

RADIOLOGY

A MONTHLY JOURNAL DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES
PUBLISHED BY THE RADIOLOGICAL SOCIETY OF NORTH AMERICA

VOL. 24

MARCH, 1935

NO. 3

THE TREATMENT OF CARCINOMA OF THE PHARYNX AND LARYNX¹

By L. H. GARLAND, M.B., B.Ch., *San Francisco*

From the Stanford University Service at the San Francisco Hospital, Department of Public Health and Stanford University Medical School

THIS paper is a summary of the technic and early results of the treatment of cancer of the pharynx and larynx by protracted fractional roentgen radiation in a rather small group of cases. Its value, if

clinics and anti-cancer centers where facilities, both pathologic and radiologic, far exceed those in the average community. Since it is not always possible for patients to gain access to those centers, the results

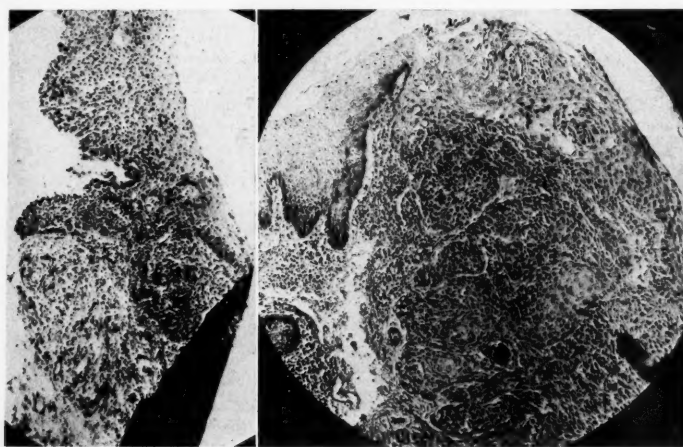


Fig. 1.

Fig. 2.

Fig. 1. Case 1. Moderately well-differentiated carcinoma of the larynx. Section near edge of tumor showing cells invading the submucosa (epidermoid carcinoma).

Fig. 2. Case 8. Well-differentiated carcinoma of the larynx. Section near edge of lesion. Slight keratinization (squamous-cell carcinoma).

any, will lie in its being a record of the results obtainable under average conditions in an ordinary city hospital of average size. Most of the literature on this subject to date consists of summaries from the larger

obtainable outside of them may, therefore, be of interest.

Types of Lesion Treated: Classification.—Most of the cases treated were either advanced or inoperable; several of the laryngeal cases were recurrent post-operative ones. None of them were regarded by the referring surgeon, rhinolaryngologist, or

¹Read before the Radiological Society of North America, at the Twentieth Annual Meeting, in Memphis, Tenn., Dec. 3-7, 1934.

TABLE I.—CLASSIFICATION OF TUMORS OF THE LARYNX AND PHARYNX

LARYNX		
Type of Cell	Well-differentiated carcinoma	A squamous-cell epithelioma (epidermoid carcinoma) composed chiefly of differentiated cells, showing keratinization and pearl formation. Often arises from the true vocal cords, the glosso-epiglottic recess, and the lateral pharyngeal wall. "Radiosensitive" but requiring large doses to cure. Usually metastasizes to glands late. Commonly graded 1 and 2.
	Poorly differentiated carcinoma	A squamous-cell epithelioma (epidermoid carcinoma) composed chiefly of anaplastic cells of the squamous variety, showing no keratinization and little if any orderly arrangement. Often arises from the superior or false cords, the aryepiglottic area, the pyriform sinus or the posterior pharyngeal wall. "Radiosensitive." Sometimes metastasizes to glands early. Commonly graded 3 and 4.
	Sarcoma	Including lymphosarcoma; rare.
Size	Stage I	Small localized tumor, not over 1 cm. in extent; usually intrinsic and often confined to one vocal cord.
	Stage II	Medium sized, localized tumor, not over 4 cm. in extent; often largely, if not entirely, intrinsic.
	Stage III	Large tumor, over 4 cm. in extent, often both intrinsic and extrinsic. All tumors with cervical adenopathy.
PHARYNX		
Type of Cell	Well-differentiated carcinoma	See above. Often arises from the posterior faucial pillars, the val-ecula and the lateral pharyngeal wall. Sensitivity and grading as above.
	Poorly differentiated carcinoma	See above. This group includes transitional cell carcinomas or lympho-epitheliomas, the latter being squamous-cell tumors which arise in contact with lymphoid tissue. "Radiosensitive." Metastasize fairly early.
	Sarcoma	Includes lymphosarcoma, so-called reticulum cell sarcoma, and other specific types, the "radiosensitivity" being in the order mentioned. Commonly arise from the oropharynx (tonsil, base of tongue, etc.).
Size	Stage I	Small tumor, up to 2 cm. in diameter.
	Stage II	Medium sized tumor, from 2 to 5 cm. in diameter.
	Stage III	Large tumor, over 5 cm. in diameter. Tumors with definite adenopathy.
Region	Epipharynx	Posterior nasopharynx, adenoid, and upper soft palate area, etc.
	Mesopharynx	Tonsil and tonsillar folds, posterior oropharynx, and base of the tongue, etc.
	Hypopharynx	Pyriform sinuses, base of epiglottis, post-cricoid area, etc.

physician as suitable for operation. There were 10 cases of cancer of the larynx and 14 of cancer of the pharynx.

its histologic appearance and that, therefore, this appearance should not be used as an index for or against radiation therapy.

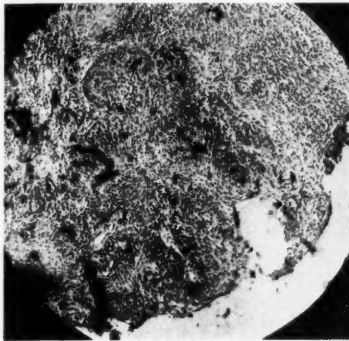


Fig. 3. Case 15. Moderately well-differentiated carcinoma of the anterior tonsillar pillar. Extensive invasion (epidermoid carcinoma).

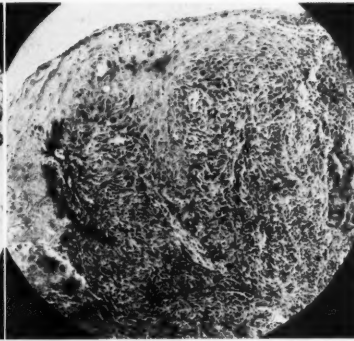


Fig. 4. Case 22. Moderately well-differentiated carcinoma of the tonsil. Extensive invasion of the submucosa (epidermoid carcinoma).

We have attempted to classify cases on three different points: (1) the histologic appearance; (2) the clinical size of the tumor, and (3) the region involved (see Table I).

Histologic grading after Broders' method has not been done by our Department of Pathology; however, most of the cases have been divided into well-differentiated or poorly differentiated ones. Since Coutard (1) believes that some poorly differentiated carcinomas may be cured by a short, intense course of roentgen therapy, while well-differentiated ones nearly always require a long, low intensity, high total dosage course, the histologic grading would appear, at first glance, to be an important guide to therapy. Unfortunately, however, in the individual case one cannot rely on the histologic prediction for purposes of estimating the dose; one has to be guided by the actual response of the tumor during treatment. Not only do some poorly differentiated epitheliomas respond slowly and require massive dosage for their arrest, but some sarcomas of the tonsil (spindle-cell reticulomas) are said to be very radioresistant (2). Cutler (3) and others (4) are of the opinion that it is no longer possible to estimate the radiosensitivity of a tumor by

Radiosensitivity does not always imply curability (*cf.* Hodgkin's disease) nor does radio-resistance indicate incurability (*cf.* small papillary adenocarcinomas). According to Broders *et al.* (5) the most common tumors of the pharynx and base of the tongue are the lymphosarcomas and the poorly differentiated epitheliomas: the most common tumors of the larynx are the well or fairly well-differentiated epitheliomas.

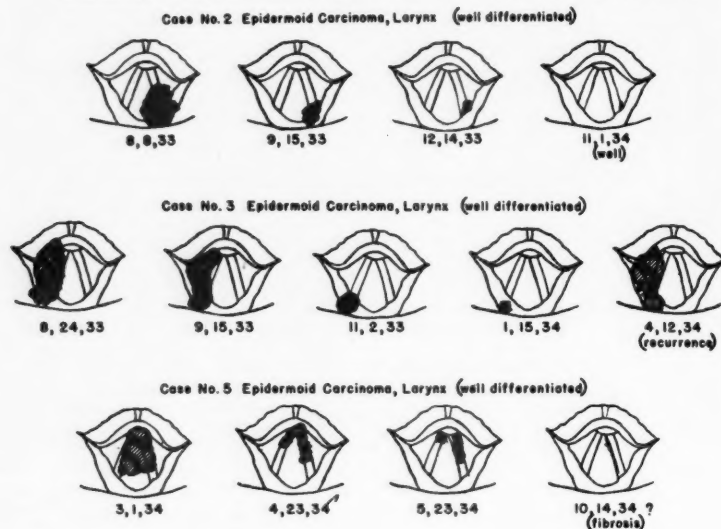
The clinical size of the tumor is quite important, since much larger doses of x-rays can be given with safety to small areas than to large ones. Coutard has observed that in his clinic very small lesions had been cured in 15 days, lesions of medium size in about 22 days, and large lesions with adenopathy in about 38 days. We realize that a tumor may be much more extensive microscopically than it appears to be clinically, but we believe that one must take the risk of treating too small a field in order safely to deliver an adequately large dose; it seems probable that, if the lesion is much more extensive than the average field used in this work, it would have been incurable anyway.

In general, therefore, it may be well to keep in mind the following points in con-

sidering the desirability of submitting a patient to curative doses of roentgen radiation:

4. The presence of much secondary infection or of invasion of cartilage or bone is said to render cure unlikely. However,

DIAGRAMS, SHOWING BEHAVIOUR OF LARYNGEAL LESIONS UNDER ROENTGEN THERAPY.



These are tracings from sketches made by the Laryngologist at time of examination.

Fig. 5. Diagram showing response of laryngeal lesions to roentgen therapy.

1. The type of the tumor. All poorly differentiated ones and some well-differentiated ones offer reasonable chances of cure.

2. The extent of the tumor. Very extensive lesions usually cannot be given adequate dosage and, therefore, only palliation should be anticipated.

3. The region of the tumor. High pharyngeal tumors are less apt to receive adequate dosage than low or laryngeal ones.

small doses, intended only to be palliative, may both save the patient from an obstructive emergency and prolong life considerably.

5. The general condition of the patient is obviously of importance; aged or debilitated persons will not usually tolerate prolonged vigorous roentgen treatment. This factor alone may prevent treatment being given to an otherwise suitable case.

TABLE II.—CLASSIFICATION OF CASES TREATED ACCORDING TO EXTENT OF LESION (ROUGHLY, INTO EARLY, MODERATE, AND ADVANCED CASES)

				Stage I	Stage II	Stage III
Pharynx	Mesopharynx	Soft palate, etc.		0	0	1
		Posterior oral area		0	0	3
		Tonsil and tonsillar pillars		0	1	5
		Base of tongue		0	0	3
	Hypopharynx			0	0	1
Larynx				0	6	4
Total				0	7	17



Fig. 6. Case. 3. Well-differentiated carcinoma right vocal cord, involving base of epiglottis and both arytenoids. Very extensive encroachment on upper laryngeal air space; emergency tracheotomy.



Fig. 7. Case. 3. Same case as in Figure 6, after treatment. Air shadow of vestibule almost normal; slight residual edema of arytenoid areas. Voice was normal.

Technic.—Preliminary films of the larynx and chest are made in each case and a biopsy is secured before or within the first week of commencing treatment. The patient is examined in conjunction with the referring surgeon or laryngologist and the position and estimated extent of the lesion are marked on each side of the surface of the neck. For localized laryngeal cases a field at least 3 cm. wider on each margin than the estimated maximum size of the tumor is used. For pharyngeal cases it is customary to use fairly large fields, as large as 14×14 cm., at least at the beginning of the course. The daily dose varies from 100 to 300 r, depending on the size of the field treated, the amount of obstruction to respiration present, and the general condition of the patient. Such a dose is given daily to alternate sides of the neck over a period of from 4 to 8 weeks.

The factors used are 200 K.V.P., 30 ma., Thoraeus filter (0.4 mm. Sn 0.25 mm. Cu, 1.0 mm. Al), effective wave length 0.125

Å., half value layer 1.5 mm. Cu, 50–60 cm. target-skin distance. The exact size and shape of the field varies in every case, and from time to time in the same case. A long, cylindrical cone is used to center accurately the beam over each field. Pieces of "radio-paque" lead rubber (2 mm. thick, absorbing 95 per cent of the primary beam) are often used to outline the exact area under treatment. The patient usually lies on his back with one shoulder moderately elevated, the projection of the beam being an oblique rather than a true lateral one.

During the fourth or fifth week, in fairly rapidly given courses, the usual "radio-epidermitis" develops, necessitating soothing skin applications, such as pieces of gauze soaked in mineral oil or smeared with boric acid ointment. At the end of the fourth week "radio-epithelitis" is usually present, necessitating sedatives and a liquid diet. Every effort is made to see that the patient takes plenty of fluids, sleeps well, and does not catch cold. Some of the

laryngeal cases, having a relatively new tracheotomy opening, are apt to develop a mild tracheobronchitis with a catarrhal discharge.

through an indwelling esophageal (post-nasal) catheter in only one case. We have had no tracheotomies except those that preceded treatment.

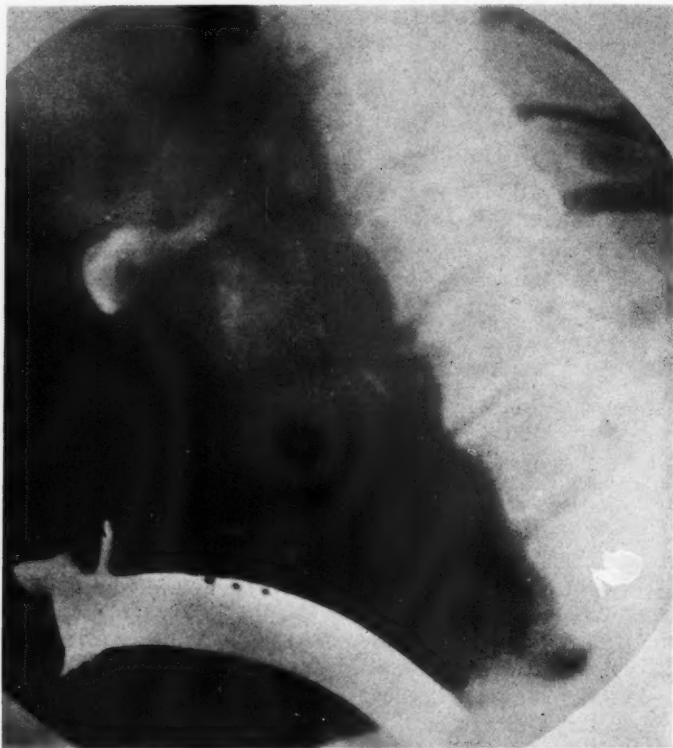


Fig. 8. Case 7. Very extensive carcinoma of larynx, recurrent post-operative. Tumor extends from base of tongue down to 2 cm. below the vocal cords. Note that the vertical extent of the tumor can best be shown by roentgen examination. This tumor shrank over 50 per cent following roentgen therapy, showing the surprisingly good palliation achievable in some advanced cases.

Depending upon the response of the tumor to treatment, the dosage may be continued. As other authors (6) have noted, the radio-epidermitis and epithelitis may commence healing and continue to heal even though treatment is continued.

The medical care of the patient is of considerable importance. We have attempted to follow Quick's (7) suggestions, especially those concerning oral hygiene, and have been gratified by the results when patients co-operated or had facilities for the frequent washings and irrigations involved in Quick's régime. We have fed the patient

In future with oropharyngeal cases we intend to suspend beside the bedside of the patient an irrigator containing potassium permanganate 1-4,000 with which the patient will irrigate his mouth four times a day (a quart to each irrigation). This would be most used during the third to fifth weeks.

Results.—The actual results in our series of cases are tabulated in Table IV. All of the 24 cases, except one, were controlled by biopsy; 22 were epitheliomas and one was questionable. This latter case and the one in which biopsy was not done were both

TABLE III.—CARCINOMAS OF THE LARYNX AND PHARYNX TREATED BY ROENTGEN THERAPY
(MODIFIED COUTARD)

Case No.	Age, sex	Site, type, and stage of lesion	Date treatment begun. Length of tr. in days	Dosage (r in air) and size of fields	Results
1	56 M	Epidermoid ca., well-diff., right side of larynx, involving pyriform sinus. Stage II	10-4-33 40 days	2,400 r left, 2,600 r right, fields av. 7.5 cm. diam. (T.D. 8,000 r/skin)*	Clinically well to date (13 months)
2	56 M	Epidermoid ca., mod. well-diff., left vocal cord. Stage II tracheotomy 8-4-33	8-10-33 50 days	4,400 r anterior, 1,000 r left, 800 r right, fields 7 × 6 cm. ant., 9 cm. diam. lateral (T.D. 7,750 r/skin)	Clinically well to date (15 months)
3	60 M	Epidermoid ca., well-diff., right vocal cord. Stage II tracheotomy 8-17-33	8-24-33 35 days	3,600 r right, 2,200 r left, fields av. 9 × 5 cm. (T.D. 7,250 r/skin)	Clinically well 7 mos. Recurred. Second course given—32 days 2,400 right, 2,500 left, fields 9-10 cm. diam. (T.D. 6,100 r/skin). Improved
4	65 M	Epidermoid ca., well-diff., left side of larynx, involving pyriform sinus. Stage II	10-4-33 40 days	2,400 r right, 2,400 r left fields 10 × 8 cm. (T.D. 6,000 r/skin)	Tracheotomy 10-13-33; bronchopneumonia 11-20-33. Died 11-29-33. Postmortem showed marked roent. changes in residual tumor tissue. Cause of death: mult. pulmonary abscesses; mediastinitis
5	57 M	Epidermoid ca., both cords, recurrent post-operative (2 months). Tracheotomy, Stage II	3-2-34 43 days	3,300 r left, 3,600 r right, fields 8 × 6 cm. (T.D. 8,600 r/skin)	Clinically arrested 8-1-34; developed mod. fibrosis about larynx; pneumonia 10-14-34 and death. No post-mortem allowed. Arrested (?)
6	71 M	Carcinoma (unclass.), left retrolaryngeal area, with cervical adenopathy. Stage III	11-15-33 26 days	3,100 r left, 3,100 r right, fields 9 cm. diam. (T.D. 7,750 r/skin)	Developed left hemiparesis 12-29-33; voice improved, but dev. metastases in spine and ribs. Died 1-14-34; no post-mortem allowed
7	59 M	Carcinoma (unclass.), larynx, advanced, recurrent post-operative (2 years). Tracheotomy, Stage III	9-26-33 32 days	2,400 r left, 2,400 r right, fields 10 × 8 cm. (T.D. 6,000 r/skin)	Developed remarkable improvement, with ability to speak; bronchopneumonia dev. foll. removal tracheot. tube. Death 1-21-34; no post-mortem allowed
8	58 M	Epidermoid ca., well-diff., right arytenoid area. Stage II	8-3-34 34 days	2,700 r right, 2,700 r left, fields 14 × 10 cm. for first half of course then 9 cm. diam. (T.D. 6,750 r/skin)	Marked improvement; voice excellent to date (one month). Patient also had stenosing lesion mid-third esoph. for which gastrostomy was done 9-20-34

TABLE III (Continued)

Case No.	Age, sex	Site, type, and stage of lesion	Date treatment begun. Length of tr. in days	Dosage (r in air) and size of fields	Results
9	63 M	Epidermoid ca., larynx. Massive tumor recurrent post-operative (3 operations) 2 years. Stage III	3-28-34 27 days	3,200 r right, 3,000 r left, fields av. 10 cm. diam. (T.D. 7,750 r/skin)	Tumor shrank and disappeared. Clinically well 11-1-34 (8 months)
10	53 M	Epidermoid ca., poorly diff., larynx, with massive right cervical adenopathy. Stage III	9-29-34 35 days	3,000 r left, 3,000 r right, fields 14 X 14 cm., then 14 X 12 cm., then 9 cm. diam. (T.D. 7,500 r/skin)	Tumor shrank; adenopathy diminished
11	77 M	Tumor post-pharyngeal wall; clinically definite carcinoma (Dr. Bacher and Dr. Graham); no biopsy. Dysphagia and hoarseness 5 months. Stage III	6-21-34 80 days	3,100 r left, 3,300 r right, fields 9 cm. diam. (T.D. 8,000 r/skin)	Treatment elongated by two-week interruption in June (bronchopneumonia). Tumor gone 11-1-34 (two and one-half months)
12	59 M	Carcinoma base of tongue, poorly diff.; bilat. cerv. adenop. Stage III	12-28-33 36 days	3,000 r left, 3,000 r right, fields 14 X 10 cm., except last six dose fields 7 cm. diam. (T.D. 7,500 r/skin)	Tumor disappeared, but pt. developed stenosing ca. mid-esoph. This received 1,700 r/o to each of four oblique 20 cm. diam. fields at 70 cm. T.S.D. in 34 days. Temp. improvement. Died 6-18-34. Postmortem showed bronchopneumonia; ca. tongue arrested; ca. esoph. (6 months)
13	65 M	Ca. base of tongue, unclass. squamous cell, rt. upper cerv. adenop. Stage III	9-19-33 33 days	2,720 r right, 2,750 r left, fields 11 cm. diam., later 9 cm. diam. (T.D. 6,830 r/skin)	Tumor shrank but did not disappear. Developed sudden throat hemorrhage 11-26-33 and died in ten minutes—(?) from shock or some vascular accident. No postmortem
14	72 M	Ca. right tonsil, large fungating (type unclass.) with cerv. adenop. rt. Stage III	1-13-33 54 days	3,600 r right, 2,700 r left, fields 10 cm. diam. (T.D. 7,800 r/skin)	Lesion, including the adenopathy, disappeared. Recurrence 4-18-34 (15 months). Further treatment refused. Alive 22 months.
15	46 M	Ca. ant. pillar left tonsil, with cervical induration. Squamous cell, well-diff. Stage II	8-14-34 36 days	3,000 r left, 3,000 r right, fields 9 cm. diam. (T.D. 7,500 r/skin)	Clinically well, 11-1-34 (one month)
16	56 M	Ca. base of tongue, rt. upper cerv. adenopathy. Unclassified. Stage III	1-12-33 50 days	4,000 r right, 2,800 r left, fields 10 cm. sq. (T.D. 8,400 r/skin)	Tumor and adenopathy shrank, leaving only tiny nodule on tongue. Pt. developed severe left craniofacial pain. Intracranial section left 9th nerve done 6-19-33, with immediate post-operative death. Arrested 4 months. No post-mortem

TABLE III (Continued)

Case No.	Age, sex	Site, type, and stage of lesion	Date treatment begun. Length of tr. in days	Dosage (r in air) and size of fields	Results
17	48 M	Ca. left side tongue, junct. mid and post. third, large, ulcerating, with left sub-max. adenop. Un-classified. Stage III	6-1-33 41 days	3,000 r left, 2,100 r right, fields 18 cm. diam. (but protecting part of parotid and laryngeal area) (T.D. 6,400 r/skin)	Tumor and adenopathy receded but did not disappear. Hemorrhage from lingual artery 9-10-33 with death. Postmortem showed ca. confined to tongue; bronchopneu. Improved 2 months
18	60 M	Ca. soft palate and post. wall of pharynx; epidermoid type. Diffuse involvement uvula and both post. faucial pillars. Stage III	9-13-33 22 days	2,000 r left, 2,000 r right, fields 10 X 8 cm. (T.D. 5,000 r/skin)	Clinically arrested to date (12 months). General health poor owing to morphine addiction. Complaints of left hemicrania (met. to middle fossa ?)
19	70 M	Epidermoid ca. left tonsil, with left cerv. adenopathy. Stage III	5-6-33 33 days	2,800 r right, 2,700 r left, fields 10 X 10 cm. (T.D. 6,900 r/skin)	Lesion shrank but small nodule persisted on post. pillar. Given 3,650 r/o to 7 cm. area at left angle jaw in Sept. (22 days) but lesion did not completely disappear. Died 4-20-34. No postmortem
20	62 M	Ulcerating tumor post. third left cheek at angle of jaw, clinically ca., but biopsy unsatisfactory (specimen inadequate). Stage II	9-15-33 17 days	3,000 r left field 9 X 6 cm. (T.D. 3,700 r/skin)	After 2 months lesion not entirely gone; given 1,200 r/o unfiltered to lesion directly (through lead tube) and 1,200 r/o externally in 12 days, Dec., 1933. Lesion clinically well 2 mos. Prostatic resection, bronchopneumonia and death, 3-12-34. No postmortem
21	78 F	Angio-epithelioma left tonsil; very large tumor. Stage II	9-14-33 18 days	3,000 r left, field 9 cm. diam. (T.D. 3,800 r/skin)	This patient had received moderate courses of radiation in Dec., 1932, and June, 1933. This fact and her age prevented more vigorous treatment. Lesion much improved but not arrested. Alive to date in relatively good condition (12 months)
22	58 M	Epidermoid ca. right tonsil with cervical adenopathy. Stage III	1-23-33 12 days	2,160 r left, 2,160 r right, fields 10 X 10 cm. (T.D. 5,400 r/skin)	Tumor shrank. Radical neck dissection 3-18-33 (few ca. areas in sections). Developed pneumonia and died on 11-10-33. Post-mortem showed no ca. in the tonsil or tongue area, but low in the cervical scar one tiny nodule was found. Arrested 9 months

TABLE III (Continued)

Case No.	Age, sex	Site, type, and stage of lesion	Date treatment begun. Length of tr. in days	Dosage (r in air) and size of fields	Results
23	73 M	Ca. right tonsil, involving rt. half base of tongue with rt. submaxillary adenopathy. Stage III	8-3-33 58 days	3,300 r left, 3,500 r right, fields 18 cm. diam. for half of course, then 9-10 cm. diam. (T.D. 8,500 r/skin)	Tumor shrank but did not entirely go away. Pt. dev. pneumonia and died 1-14-34 (4 months). Postmortem showed very little tumor tissue in the tonsil (looked "non-viable"); glands neg.
24	66 M	Epidermoid ca. post. portion of floor of mouth; fairly well diff. Submax. adenop. Stage III	11-24-33 35 days	3,100 r right, 3,000 r left, fields 14 X 10 cm. for three-fourths of course; 9 cm. diam. for remainder (T.D. 7,600 r/skin)	Tumor shrank and was cauterized 12-29-33; eight gold radon seeds inserted 3-15-34; bleeding required ligation left ext. carotid 6-8-34. Dev. bronchopneumonia and died 6-15-34. Postmortem showed tumor not arrested

* T.D. is the total dose to all fields, including back-scatter (estimated at approximately 25 per cent for the average 10 cm. diameter neck field). It is given purely for ready comparison of our doses with those mentioned in the French and other literatures.

clinically definite carcinomas. While clinically cured, death from post-prostatectomy complications removed the "questionable case" from the group of arrested ones now living. The patient without biopsy is alive and well (only three months have elapsed since the end of treatment).

There were 14 cases of carcinoma of the pharynx; seven were not arrested by treatment and seven were clinically arrested at the end of their course. One of these recurred (after 15 months), and three died of intercurrent disease, leaving but three cases clinically well at the time of making this report. The three cases that died of intercurrent disease are as follows:

Patient with cancer of base of tongue (No. 12) who died six months after the end of treatment from an independent cancer of the mid-esophagus and bronchopneumonia. Palpation and inspection (removal not permitted) of the tongue showed no tumor.

Patient with cancer of the posterior oral area (No. 20) who died two months after the end of treatment, from pneumonia complicating prostatic resection. No post-

mortem was allowed. A clinically arrested case.

Patient with cancer of the tonsillar area (Fig. 4) involving the base of the tongue (No. 22) who died nine months after the end of treatment from pneumonia complicating a simple cold. At autopsy, careful examination of the tonsillar area and tongue revealed no evidence at all of carcinoma, but at the base of a long left cervical scar (the patient had a bloc dissection following roentgen therapy) a tiny microscopic nodule of carcinoma was discovered after prolonged search.

There were 10 cases of carcinoma of the larynx; five were not arrested by treatment, and five were clinically arrested. It is only fair to point out here that three of the five not arrested were very advanced, indeed hopeless cases. One of the arrested cases recurred, seven months following treatment (Fig. 5).

Complications.—There was no mortality directly attributable to the roentgen treatment in this series of patients. No late necroses of cartilage or bone, nor pharyn-

geal obstructions developed. One patient (No. 5) developed some fibrosis about his tracheotomy opening about two months following treatment: he had had an extensive cancer of the larynx, recurrent two months after operation by a skilled laryngologist, and also much secondary infection about the tissues of his neck. His tumor disappeared following treatment, but thick fibrous tissue about the mid-laryngeal area

prevented removal of the tracheotomy tube. He developed pneumonia four months following treatment and died; no autopsy could be obtained.

Two of the pharyngeal cases developed severe hemorrhages from the tumor area: one, one month following treatment; the other, four months following treatment. However, during the same period, two other cases that received little or no radia-

TABLE IV.—ROENTGEN THERAPY RESULTS

Lesion	Cases treated	Improved but not arrested	Arrested but recurred	Clinically well	Arrested but died of intercurr. disease	Dead with or of cancer
Mesopharynx	13	7	1	2	3*	6
Hypopharynx	1			1		
Larynx	10	5	1	4		4

Total cases treated..... 24
 Clinically arrested at end of tr..... 12 (50%)
 Recurrence to date..... 2 (16%) one at 7, one at 15 months.
 Clinically well to date..... 7 (29%)
 Well over 8 and up to 18 months..... 4 (16%)

* See text.

TABLE V.—COMPARISON OF THE RESULTS OF TREATMENT OF CANCER OF THE PHARYNX AND LARYNX*

1. Roentgen Therapy

Author	Lesion	No. cases	Results	
			Primary healing	Later results
Coutard	Ca. tonsil	46		12 or 26% (4 years and over)
	Hypopharynx	89		12 or 13% (4 years and over)
	Larynx	77		22 or 28% (4 years and over)
Schinz	Pharynx and larynx	116	65 or 56%	40 or 34% (9 mos.-3 yrs.)
Maisin	Pharynx	74	25 or 34%	19 or 26% (2 years and over)
Lenz	Pharynx and larynx	31		14 or 45% (9 mos.-2 yrs.)

2. Surgery

Patterson	Pharynx	50	24 or 48%	12 or 24% (4 years and over)
New, <i>et al.</i>	Pharynx and larynx and tongue	176		32 or 18% (5 years and over)
Colledge	Larynx	79	33 or 41%	11 or 14% (4 years and over)
Clerf	Larynx	58		18 or 31% (5 years and over)

* It is to be remembered that most of the cases treated by roentgen therapy were extensive or late cases, while most of the surgical ones were operable or early ones.

tion (one case, only 600 r to each side, the other, none at all) developed similar severe hemorrhages, so that it is my belief that the bleeding may have been due to inevitable infiltration by tumor and not to roentgen necrosis of vascular walls.

Severe oral dryness with varying degrees of disturbance of taste occurred in several of the cases. One patient (No. 14) complained that this disturbance of taste made him more miserable than the original tumor (a fungating tonsillar carcinoma, with cervical adenopathy). Slight atrophy of skin with patchy telangiectasis appeared in a few of the cases that received more than 4,000 r/air to one area.

Discussion.—In cases in which the tumor has not almost entirely disappeared at the end of the planned amount of radiation, or when skin tolerance seems to have been reached, it is very difficult to decide how much more should be given. It is also difficult to treat patients as vigorously or as consistently as one would like to do. The great tendency in this work seems to be to "ease off" in dosage; this is well seen in Coutard's cases and is apparent from close

study of the detailed case reports of other authors. To refresh our memory on what Coutard has written under the heading "dosage and cancericidal effects" we transcribe the following from his 1932 paper:

"To sum up, if the field is small and if the distribution of irradiation is accomplished in the maximum period of 15 days, we consider that the doses capable of provoking the destruction of epithelial cells correspond, for the skin, to 45 H. (about 4,500 r); for the mucous membranes, to 35 H. (about 3,500 r). These doses, which should necessarily be modified according to intervening infection, deep infiltration, or adherence to the cartilages, have permitted us to cure some cancers more easily because of their greater radiosensitivity. In order to attain these doses in the area of the lesion to be destroyed, we have been obliged to utilize, for the combined portals of entry, a total dose nearly double the preceding one.

"We have seen that in the treatment of pavement epitheliomas there is no relation, up to a certain limit, between the doses received and the frequency of cures, regardless of the degree of radiosensitivity. Our patients have been cured with doses between 7,000 and 8,000 r, or from 70 to 80 H. When the doses have reached 90, 100, and 150 H., there was no cure; on the contrary, aggravation of the patient's condition

TABLE VI.—COMPARISON OF ROENTGEN TECHNIQS REPORTED*

Author	Lesion	K.V.	Filter, mm.	Dist. cm.	Fields, cm.	Intensity and daily dose (r in air)†		No. of fields	No. of days of treatment	Total dose (all fields added—r in air)†
						r per min.	r per day			
Coutard	Mesopharynx	200	2 Cu or Zn 3 Al	60 av.	10 × 15	3	160-480	2-4	17-40 (av. 35)	4,000-6,500 (av. 5,200)
	Hypopharynx	200	3 Al	60 av.	10 × 15 to 10 × 20	3	160-480	2-4	8-47 (av. 28)	3,500-6,500 (av. 4,800)
	Larynx	200	3 Al	60 av.	7 × 7	3	160-480	2	9-39 (av. 18)	4,000-6,500 (av. 5,000)
Schinz	Pharynx and larynx	200	2 Cu	50 av.	?	3	300	2	15-32 (av. 20)	6,400 av.
Lenz	Pharynx and larynx	200	1.86 Cu 1 Al	50	6 × 8 to 10 × 10	10	300-450	2-4	16-44 (av. 31)	5,600-9,400
Mattick	Larynx	200	3 Cu	50 to 80	10 × 15	15	140	1	15-?	2,000 up (one ant. field)
Maisin	Pharynx Tonsil sa.	200	2 Cu	65	?	3	400	2-3	21-35 (av. 24)	3,500 av.
		200	1 Cu	40	?	.	240-400	2-3	10-15	3,300 av.
Kaplan	Pharynx and larynx	200	2 Cu 1 Al	60	10 × 15	5	400-500	2	21-30	6,800-8,800
Author	Pharynx and larynx	200	Thor.	50 to 60	14 × 14 to 7 diam.	32	100-300	2	12-60 (av. 35)	6,000 av.

* Many of these technics have undergone considerable modification since the time they were reported; however, they are of interest since most existing roentgen statistics are built from them.

† Recalculated, where necessary, from figures published with back-scatter. To obtain the approximate "Skin dose" add 25 per cent to these figures.

and increased rapidity of recurrence have been the rule.

"Under the conditions in which our treatments were conducted, the cancericidal effects did not increase proportionately with the doses, beyond a certain value.

"Neither do the cancericidal effects increase proportionately with the time of treatment—quite the contrary. The real or apparent loss of radiosensitivity (immunization) of the cells of squamous epithelioma is often appreciable about the thirtieth day after beginning of the treatment. In the same way, the epithelial radiolesions of the skin and mucous membranes are more difficult to provoke (even when the doses are slightly increased) the longer the treatments have lasted."

Beside the proper total dose, the proper period of time over which the treatment should be given is difficult to decide. When visiting Coutard's clinic two years ago I observed him giving as little as 50 r per day, stating that he would continue treatment for as long as 14 weeks: he stated that he was giving as high as 7,000 r to one side of the neck and 5,000 r to the other. He admitted that his skin and mucous membrane reactions in these particular cases would not be nearly so marked as in his earlier cases and implied that his cures would possibly be fewer thereby. It is worth remembering that the classical Coutard epidermitis is produced by 4,500 to 5,000 r/skin given in 10 days of two daily sittings, each one hour long; the cutaneous epithelium is completely gone on about the twenty-seventh day and completely repaired on about the forty-second day.

Kaplan, *et al.* (6) believe that under proper conditions the full course should be completed in 21 days; under such conditions the epidermitis will usually commence on the eighteenth day and terminate on the twenty-sixth, and epidermitis will commence on the twenty-sixth and terminate on the fortieth day. These authors believe that the extension of the treatment over too long a time, "that is, from 30 to 35 days," results in milder reactions and fewer cures.

How wide a field should be used? Realizing how much the general discomfort of the patient increases with the amount of radia-

tion given and the size of the field used, and yet remembering how important it is to use relatively large fields to secure adequate depth dosage as well as wide enough distribution of the beam, one has always to compromise on this question. On the whole, it would seem advisable, especially with pharyngeal cases and extensive laryngeal cases, to commence with a large field, at least on the same side as the lesion; in actual practice we have usually ended up with fields from 9 to 7 cm. in diameter. With necks of average size and fields 10 cm. in diameter, using the factors above mentioned, the amount of back-scatter to the skin is approximately 25 per cent. Since our estimations of back-scatter, tissue dose, and transmitted dose are all of questionable significance, we have not attempted to estimate actual tumor doses in the individual cases. When means become available to do this we shall attempt it, since it is obviously of considerable importance.

The major modification which we have been compelled to make in our technic (as compared to Coutard's) is in the r per minute intensity. Coutard (1), Schinz (8), Zwerg (9), and others believe that the r per minute intensity should be very low, not more than 5 r per minute. In addition, Coutard treats some of his patients twice a day so as to prolong the time under treatment. On the other hand, Pack and Quimby (10) on experimental grounds, and Lenz (11), Mattick (12), and other authors (13) on clinical grounds believe that satisfactory results can be secured with an intensity of from 10 to 30 r per minute. Most of our cases have been treated with an intensity of 32 r per minute.

A review of our small series of cases suggests that perhaps we should have treated some of them more rapidly, much more rapidly (*e.g.*, 24 instead of 36 days) or that we should have given them larger doses (*e.g.*, up to 4,500 r to each side). It is noteworthy that none of them suffered necrosis of cartilage or bone.

Other undecided but perhaps less important points include the question of the influence of wave length upon biologic

effect. Since the results of both animal and clinical experimentation are conflicting, we must fall back on clinical impressions. There is no question but that the majority of workers favor thick filters, that is, filters giving an effective wave length of 0.12 to 0.11 Å. We have used a Thoraeus combined tin filter instead of 2 mm. Cu because of its relatively increased efficiency (giving approximately 30 per cent more transmission than 2 mm. Cu but a similar "hardness"). We think or imagine that the cutaneous reactions are less severe with it than with 0.5 mm. Cu, but we realize that there are many who believe that the reactions are equally severe with either filter.

The question of pre-biopsy radiation is also a moot one. It is interesting to note a recent statement by a well-known nose-and-throat surgeon (14), urging that such should always be done. Personally, we regard it as a logical procedure.

Finally, the question of what constitutes the most judicious combination of radiation and surgery arises. Schinz (8) believes, as far as laryngeal tumors are concerned, that well-differentiated intrinsic epitheliomas with fixation of the cord can be treated surgically or radiologically. He thinks that all other laryngeal tumors should be treated radiologically. Like Coutard, he favors radiation in early cases on account of the better conservation of the voice. Coutard believes that when there is much infiltration of the laryngeal muscles, resection, followed by protracted roentgen therapy, will give better results on the whole than roentgen therapy alone. D. Harmer (14) advises, for operable tumors, a combination of short-course pre-operative radiation, surgery, and, starting about ten days later, long-course post-operative radiation. For all inoperable ones he recommends radiation only.

For pharyngeal tumors there is little doubt that radiation is the superior method of treatment. In early lesions the choice must depend on the facilities available and the relative skill of the surgeon and the radiologist. As Bloodgood (15) recently stated: "X-rays are no longer looked on as

a last resort." One has only to see the results obtainable with properly administered radiation to suspect that the day of extensive mutilating operations is passing; no longer must one tell a patient that the only chance of cure in primary malignant disease of the oropharynx lies in an operation which may sacrifice half of the jaw. However, while proper radiation treatment requires as much judgment and care and considerably more patience than surgical treatment, Cade's remark that "competent surgery is still preferable to incompetent radiation" seems worth recalling to mind.

SUMMARY

Many cases of malignant disease of the larynx and pharynx can be arrested and apparently cured by adequate, carefully administered, roentgen therapy.

None of the present series of cases has been observed for a period of five years and, therefore, the number of "clinical cures" cannot be stated. However, it may be pointed out that 12 out of 24 cases showed primary healing, and 7 out of 24 cases are clinically arrested at the time of making this report (two months to one and one-half years) and that some of the others received remarkable palliation.

No patients died from causes directly attributable to the roentgen therapy in this series of cases. No late necroses of cartilage or bone and no laryngeal or pharyngeal obstructions due to radiation were observed.

BIBLIOGRAPHY

- (1) COUTARD, H.: Roentgen Therapy of Epitheliomas of the Larynx. *Am. Jour. Roentgenol. and Rad. Ther.*, 1932, **28**, 313.
- (2) MAISIN, J., VAN DEN WILDENBERG, L., and VASSILIADIS, H.: Radiological Treatment of Some Cancers of the Oropharynx. *Jour. Laryngol. and Otol.*, 1933, **48**, 479.
- (3) CUTLER, MAX: The Problem of Radiosensitivity. *Jour. Am. Med. Assn.*, 1934, **103**, 1204.
- (4) CADE, S.: Radiation Treatment of Cancer of the Mouth and Pharynx. *Lancet*, 1933, **2**, 4.
- (5) NEW, G. B., BRODERS, A. C., and CHILDREY, J. H.: Highly Malignant Tumors of the Pharynx and Base of the Tongue. *Surg., Gynec., and Obst.*, 1932, **54**, 164.
- (6) KAPLAN, I., FRIEDMAN, M., ROSH, R., and BRAESTRUP, C. B.: Protracted External Irradiation in the Treatment of Carcinoma of the Mouth and Throat. *RADIOLOGY*, 1934, **23**, 339.
- (7) QUICK, DOUGLAS: Management of Cancer of

- the Mouth and the Cervical Lymphatics. *Am. Jour. Roentgenol. and Rad. Ther.*, 1934, **31**, 366.
- (8) SCHINZ, H. R.: Operative u. radiotherapeutische Behandlung der Krebse. *Strahlentherapie*, 1933, **46**, 7.
- (9) ZWERG, H. G.: Die Theoretischen, experimentellen Klinischen u. wirtschaftlichen Grundlagen der protrahiert fraktionierten Röntgenbestrahlung Maligner Tumoren. *Strahlentherapie*, 1932, **43**, 201.
- (10) PACK, G. T., and Quimby, E. H.: The Time-intensity Factor in Irradiation. *Am. Jour. Roentgenol. and Rad. Ther.*, 1932, **28**, 650.
- (11) LENZ, M.: Roentgentherapy of Malignant Neoplasms of the Pharynx and Larynx. *Jour. Am. Med. Assn.*, 1932, **99**, 1840.
- (12) MATTICK, W. L.: Heavily Filtered High Voltage X-irradiation in Cancer Therapy. *Jour. Am. Med. Assn.*, 1932, **99**, 3157.
- (13) MARTIN, H. E., and McNATTIN, R. F.: The Treatment of Carcinomas of the Pharynx, Tonsil, and Extrinsic Larynx by Divided Doses of Radiation Therapy (unpublished). Read at First Am. Congress of Radiology, 1933.
- (14) HARMER, DOUGLAS: See Discussion of Webster (ref. 19 below), p. 914.
- (15) BLOODGOOD, J. C.: See Discussion of paper by Cutler, Max (*vide* ref. 3 above).
- (16) PATTERSON, NORMAN: Malignment Disease of the Oropharynx. *Jour. Laryngol. and Otol.*, 1933, **48**, 463.
- (17) COLLEDGE, L., and PEACOCK, R.: An Analysis of 126 Cases of Malignant Disease of the Upper Air Passages Treated during a Period of Ten Years (1921 to 1930). *Jour. Laryngol. and Otol.*, 1932, **47**, 161.
- (18) GORDON-TAYLOR, G.: Malignant Diseases of the Oropharynx. *Jour. Laryngol. and Otol.*, 1933, **48**, 463.
- (19) WEBSTER, J. H. D.: The Protracted-fractional X-ray Method (Coutard) in the Treatment of Cancer of the Larynx. *Proc. Roy. Soc. Med.*, 1934, **27**, 901.
- (20) STEWART-HARRISON, R.: Maligne Pharynx und Larynx tumoren Vorläufige Gesamtergebnisse der protrahiert-fraktionierte Röntgenbestrahlung von 1929 bis ende 1931. *Schweiz. med. Wchnschr.*, 1933, **14**, 41.
- (21) SCHINZ, H. R., and ZUPPINGER, A.: Kurzer Bericht von Arbeiten und Resultaten auf dem Gebiet der protrahiert-fraktionierten Röntgenbestrahlung von malignen Gesahwulsten. *Schweiz. med. Wchnschr.*, 1932, **13**, 545.
- (22) ZUPPINGER, A.: Protracted Fractional Method of Roentgen Therapy. *Am. Jour. Roentgenol. and Rad. Ther.*, 1931, **25**, 784.
- (23) CLERF, L. H.: Analysis of 58 Cases of Cancer of the Larynx Treated by Laryngofissure. *Arch. Otolaryng.*, 1934, **19**, 653.
- (24) LENZ, M., COAKLEY, G., and STOUT, A.: Roentgen Therapy of Epitheliomas of the Pharynx and Larynx. *Am. Jour. Roentgenol. and Rad. Ther.*, 1934, **32**, 500.

INTRA-ORAL CANCER AND ITS TREATMENT¹

By ORVILLE N. MELAND, M.D., F.A.C.S., *Los Angeles*

THIS subject is not a new one with us—it has been presented on two previous occasions (1 and 2)—but in this communication we are giving a review of the work carried out in the years 1930, 1931, and 1932. It was prompted by a recent report from the Curie Institute (3) and its purpose is to draw some conclusions that may be of future guidance in treating patients with this disease.

In order to facilitate the case analysis, patients have been segregated into two large groups: (A) Those in which there were lesions of the tongue alone, of which there were 69 cases; (B) Those in whom the malignancy was on the buccal surfaces, palate, and alveolar regions, of which there were 26 cases. For further ease in study these groups were subdivided into classes as given below:

TABLE I

Class I.	Primary lesion less than 2 cm. in diameter
Class II.	Primary lesion over 2 cm. in diameter
Class III.	Primary lesion associated with enlarged lymph nodes
Class IV.	Recurrent lesion after operation

Diagnosis.—The diagnosis of malignancy in the oral cavity seems simple enough to an experienced observer but to the average physician it offers much difficulty. In early borderline cases confusion is bound to arise at times, but too often cancer is mistaken for acute inflammatory lesions such as trench mouth or for one of the manifestations of syphilis. In the minds of many men a smear or a blood Wassermann seems to clinch the diagnosis and suggest the treatment. Many patients are treated for weeks by local applications and intravenous arsenicals, even in the presence of an advancing lesion before a biopsy is even con-

sidered. It is excusable to treat a patient for a week or two but when no improvement takes place one may rest assured that something exists beside the condition for which treatment is given. When taking smears and blood for a Wassermann, why not make the biopsy a routine procedure? It is a simple one, carried out under local anesthesia, and from our observation as well as from the publications of others it does not seem to lead to dissemination where proper treatment is instituted immediately. After all, the absolute diagnosis rests on biopsy and biopsy alone; the sooner this lesson is impressed on the profession and laity alike, the sooner will we see earlier diagnosis and improvement in clinical results.

In the material we are studying we find that in Group A, biopsies were done in 47 patients, and in all of these a diagnosis of squamous-cell epithelioma was made. In Group B, we have 21 patients in whom a pathologic examination confirmed the clinical impression—all sections were put down as squamous-cell epithelioma except one, which was reported as a small round-cell sarcoma. In the remaining patients, because they were in such an advanced state of the disease, the diagnosis was made by clinical examination alone—most of these individuals were not treated.

Prognosis.—Prognosis is dependent on a number of factors, for instance, such associated complications as infection and syphilis are very important. Extensive purulent infections result in engorgement of the lymph vessels which favors early metastatic emboli into the nodes, diminishing the chances of cure: syphilis also influences the outcome. In our patients, seven had a previous history of syphilis which was verified by a positive Wassermann. All of these patients were rather advanced in their disease but despite ener-

¹ Presented before the Radiological Society of North America at the Twentieth Annual Meeting, at Memphis, Tenn., Dec. 3-7, 1934.

getic treatment both by radiation and electrosurgery, not one recovered.

The two outstanding conditions of especial significance are the size of the lesion and the histologic picture. From the standpoint of extent of the lesion we have prepared Table II: Table III gives the influence of pathology.

TABLE II

Group A	Cases	Well	Not treated		Dead
Class I	25	11 (44%)	(60%)	7	7
Class II	19	5 (26.3%)	(45%)	8	7
Class III	19	0 (0%)	(0%)	8	11
Class IV	6	2 (33%)	(49%)	1	3
	69	18		24	27

Group B	Cases	Well	Not treated		Dead
Class I	10	9 (90%)		0	1
Class II	5	4 (80%)		0	1
Class III	9	2 (22%)		0	7
Class IV	2	0 (0%)		0	2
	26	15		0	11

TABLE III

Group A	Cases	Living	Dead	
Ungraded	28	10 (35%)	18	
Grade I	5	4 (80%)	1	
Grade II	12	3 (25%)	9	
Grade III	1	0 (0%)	1	
Grade IV	1	0 (0%)	1	
	47	17	30	

Group B	Cases	Living	Dead	
Ungraded	11	10 (90%)	1	
Grade I	2	1 (50%)	1	
Grade II	5	4 (80%)	1	
Grade III	1	0 (0%)	1	
Grade IV	1	0 (0%)	1	
Sarcoma	1	0 (0%)	1	
	21	15	6	

As a rule, the smaller the lesion, in the absence of secondaries, the better the chance of recovery. Likewise from a pathologic standpoint, the lower the degree of malignancy the less chance of metastasis and the greater the opportunity of recovery. High degree malignancies are not very common and rarely recover, but low grade malignancies, even in the presence of metastasis or recurrence when combined

electrosurgery and radiation are used, may be followed by recovery.

Treatment.—The treatment of the primary lesion in these patients has been varied according to a number of conditions. Briefly, they are tabulated as follows:

1. Condition of the patient.
2. Pathologic diagnosis and grading of the tumor.
3. Extent of the primary lesion.
4. Presence of metastatic nodes which are operable or inoperable.
5. Presence of complicating diseases as marked secondary infection, syphilis, and diabetes.

No hard and fast rules can be laid down, especially in the aged, since we must remember that though we are treating cancer we are also treating a patient. In some, palliation alone is all that can be hoped for even though the primary lesion is technically curable, since the general health precludes anything radical. On the other hand, a patient may be in excellent condition physically but the disease may be so malignant and extensive locally that curative and radical treatment is not justifiable. When conditions are favorable, we make use of radiation in any or all of its forms as well as electrosurgery. The methods which we have used are as follows: (1) Radon gold seeds alone; (2) Platinum radium needles alone; (3) Surface radium; (4) Electrosurgery alone; (5) Combined radiation and electrosurgery.

In the tongue, after extended use of both needles and seeds, we have come to the conclusion that seeds are preferable. We realize that this is not in accord with the views of some men in England, France, and this country who use needles to the exclusion of seeds. Needles do give a more constant and a better quality of radiation because of the higher filtration, but because the trauma incident to their insertion is greater, they carry a greater risk of infection than do seeds. The discomfort to the patient is more marked since they easily fall out and must be replaced: seeds, on the other hand, are easily inserted and need not be watched. Furthermore, the

use of needles requires hospitalization, with its increased expense, an item of importance at present to every patient.

Secondary Nodes.—What should be done with suspected and palpable nodes is a big problem: a question which was discussed in two previous publications (1 and 2). That a great difference of opinion still exists can be seen from the reports of the California Cancer Commission on this matter (4). This report represents a cross-section of world opinion on the subject by men who are engaged in this particular type of work. In conformity with our previous opinions, we are still conservative in our attitude. The lymph node has a definite function to perform; it acts as a barrier, and should be treated as such. We do not feel that every case should have a radical neck dissection unless there are definite indications for it, since many patients do not develop nodes at any time. As a general rule, we believe that each case should be individualized, but the following method is usually our accepted mode of attack.

1. In the clinical presence of a primary lesion and no visible or palpable nodes in the neck, the lymph draining areas are given prophylactic irradiation by means of high voltage x-ray to each side of the neck. The patient then reports for a check-up at stated intervals; if nodes develop, a neck dissection is advised. The *rationale* of such a procedure is justified by the experience of Widmann (5), who found that in patients with epithelioma of the lip where no nodes were palpable only 17 per cent developed metastasis, while 51 per cent of the non-irradiated individuals developed uncontrollable cervical lymph node metastasis. Prophylactic irradiation does not interfere with a later neck dissection if nodes develop and surgical interference is necessary. The following case is illustrative.

L. B., aged 41 years, reported to the hospital on Feb. 12, 1932, with a lesion on the buccal surface of the left cheek, 2.5×3 cm. in size, which had been present four months. No nodes were palpable. Biopsy

showed squamous-cell epithelioma, Grade II.

On Feb. 15, 1932, 7 platinum needles with a total content of 10.1 mgrs. of radium were inserted under the lesion, giving a total dosage of 969.6 mg.-hr. over 96 hours. In the latter part of March the lesion had completely disappeared. He was then given x-radiation, a total dose of 1,190 r under the chin over a two-week period, with the following factors: 30 cm.; 100 K.V.; 4 ma., 0.25 mm. Cu plus 1 mm. Al filter. Three nodes developed near the left submaxillary gland.

In June, the submaxillary and submental regions were cleaned out by means of the endotherm, with primary healing. The nodes showed the presence of metastasis. In October, 1934, he was well.

2. In cases in which the patient has palpable but not fixed nodes in the neck, both sides are treated with x-radiation. If the section of the primary lesion shows a high grade of malignancy, only radiation is used. In the lower grades, if the primary lesion is controlled and the nodes are still palpable, then the two procedures have been adopted.

(a) *Radical dissection of the neck by means of the endotherm, followed by the implantation of platinum needles for a few days.*—The following case is an illustration.

J. H. P., aged 51 years, reported on Nov. 9, 1932, with a lesion on the buccal surface of the right cheek, 2 cm. in diameter and 0.5 cm. thick, which had been present six months as a sore. He had been treated for syphilis and trench mouth by two physicians. On examination, besides the primary lesion, he had two nodes in the region of the right submaxillary region, the largest being 3 cm. in diameter. Biopsy showed squamous-cell epithelioma, Grade II.

On Nov. 17, 1932, six gold seeds of 12 mc. were plunged around the growth of the primary lesion. The mouth was healed on Jan. 13, 1933.

The secondary nodes were treated by x-radiation to the right side of the neck, 1,250 r, over a 10×10 cm. area, from Nov.

9 to 16, with the following factors: 50 cm., 200 K.V., 4 ma., 0.5 mm. Cu plus 1 mm. Al. On Jan. 23, 1933, under Avertin anesthesia, a Butlin operation on the right side of the neck was done by means of endotherm. Four platinum needles were inserted around the digastric muscle, the total dosage for 72 hours being 288 mg.-hrs. On March 22, 1933, no pathology was present. In October, 1934, he was well.

(b) *Exposure of the nodes and implantation of radon.*—The following case is an illustration.

C. P., aged 54 years, reported on June 2, 1932, that for six months he had suffered with a sore on the tongue which had been treated by carbolic acid. On examination, there was a lesion 3.5 cm. long involving the entire left side of the organ, also, a node 1.5 cm. on the left side of the neck over the carotid bifurcation. Biopsy showed squamous-cell epithelioma.

On June 10, 1932, 18 gold seeds containing 2 mc. each were inserted into the primary lesion of the tongue. On September 30, the tongue was healed. The secondary lesion was given x-radiation over both sides of the neck, 1,200 r to the left side, 900 r to the right side, with the following factors: 50 cm., 200 K.V., 4 ma., 0.5 mm. Cu plus 1 mm. Al. Treatment was given from June 2 to 9, 1932.

On March 8, when the node did not disappear it was exposed by electrosurgery and 13 gold seeds containing 19.5 mc. were inserted around and into the node. A severe reaction resulted but was followed by healing. In November, 1933, osteomyelitis of the left mandible developed which led to sequestration of the angle of the jaw. In October, 1934, the patient was in good condition except for loss of a part of the jaw; the tongue was healed and the node in the neck has disappeared.

3. In fixed inoperable nodes we have relied on x-radiation alone, radium packs, radon seed implants, or radium needles.

As a general rule in the patients we have studied, in whom the nodes in the neck are involved, x-ray and surface radium alone have not been sufficient to control the

disease even when the primary lesion is cured. We have, however, patients who have recovered when a combined radiological and surgical attack with or without the use of seeds and needles has been used. Whether the technic as described by Coutard will improve external radiation results remains to be seen. We have patients under observation in whom nodes have entirely disappeared after the use of his technic but the observation time is too short at present to offer any opinion as to the ultimate outcome.

Results of Treatment.—Reference to Tables II and III gives the result of treatment. By careful selection of the method of treatment, many of these patients recover: the outcome is influenced to a great extent by the side of the lesion, its location, and the histologic picture. We cannot change the histologic findings nor the degree of malignancy, but we can by educational methods hope to influence the size of the lesion by earlier recognition. Laymen are prone to disregard trivial lesions in the mouth until quite advanced, but they alone are not to blame. The first medical adviser has often been an advocate of "watchful waiting" and has lulled the patient into a false sense of security which has pushed him out of the curable class into that of the incurable. Professional education will bring desired results if early biopsy is stressed in all doubtful cases.

SUMMARY

1. Improvement in the cure of intra-oral cancer may be expected where biopsy is carried out early: it gives the absolute diagnosis and suggests the type of treatment which must be varied to suit the individual.

2. Interstitial radiation, either in the form of gold radon seeds or platinum needles, for the primary lesion is the therapy of choice; it must be supplemented by electrosurgery where indicated.

3. Highly filtered x-radiation to the lymph-bearing areas and lymph nodes is indicated as a prophylactic in all cases; in those in which operable nodes are present,

x-radiation supplemented by radon implants to the nodes or electrosurgical dissection offer the patient the best we know of at present.

4. X-radiation for palliative purposes is indicated in the inoperable group.

REFERENCES

(1) SOILAND, ALBERT, and MELAND O. N.: Intra-oral Cancer and its Treatment. Calif. and Western Med., August, 1930.

(2) MELAND, O. N.: The Treatment of Metastatic Involvement of the Neck Secondary to Intra-oral Cancer. Am. Jour. Roentgenol. and Rad. Ther., July, 1931.

(3) ROUX-BERGER: Cancer of the Tongue. Statistics from the Curie Foundation. Bull. et Mem. Soc. Nat. de chir., 1932, pp. 1343-1353.

(4) PFLUEGER: Treatment of Neck Glands in Cancer of Lip, Tongue, and Mouth. Calif. and Western Med., December, 1933.

(5) WIDMANN: Carcinoma of the Lip: Results of Roentgen and Radium Treatment. Am. Jour. Roentgenol. and Rad. Ther., August, 1934.

THE EVALUATION OF THE ROENTGEN TREATMENT OF LARYNGEAL CARCINOMA¹

REPORT OF CASES

By I. SETH HIRSCH, M.D., and SAMUEL M. BAUM, M.D., *New York City*

From the Radiation Therapy Department, Beth Israel Hospital

INTRODUCTION

THE evaluation of the therapeutic methods utilized for this disease is not an easy task. There are several reasons for this. Firstly, even to-day, the technic of radiation therapy has not yet been standardized. The results which any therapist is able to show at present are, therefore, in a sense experimental. Secondly, usually none but the most advanced and hopeless cases have been submitted for radiation treatment. The early intrinsic cases of carcinoma, cases which surgeons consider suitable for operation, are seldom subjected to radiation. Thirdly, there is much to be desired in the manner in which the results are summarized statistically.

Despite all this, such an analysis of the literature as is now possible would indicate that results obtained by radiation treatment in the advanced and hopeless cases are encouraging. Many sufferers have been rendered clinically free of the disease, or have had their lives prolonged in relative comfort. It is on the basis of experience, mainly, with this group, that the merits of radiation therapy as a means of controlling carcinoma of the larynx have been established. In the group not completely in the category of the inoperable, small as it is, the results obtained seem to warrant the statement that irradiation produces end-results as good as those obtained by surgical treatment, with the additional gain, the preservation of the voice. The combination of irradiation and surgery

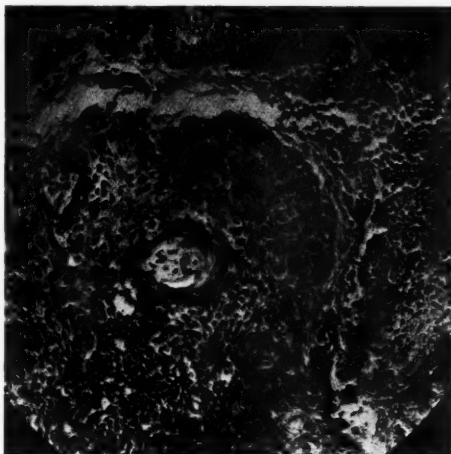


Fig. 1. Squamous-cell carcinoma with hornification, partly necrotic.

seems to give better results than surgery alone.

ACHIEVEMENTS OF ROENTGEN THERAPY IN LARYNGEAL CANCER

Definite progress with this form of therapy is a very recent accomplishment. In 1922, Gunsett reported that he had treated two patients with high voltage x-rays, one remaining clinically free for a period of eight years. Ten years later (1932) he again reported, on a total of 33 cases (including the earlier ones), 23 being advanced and 10 intrinsic. One patient had lived nine years, two for four years, and five for three years—a total of nine survivals.

In 1922 also, Parès, in France, claimed to have cured five out of ten cases, and Pfahler utilized high voltage x-ray therapy before laryngotomy or other surgical measures. In 1923, Coutard and Hautant reported that 58 per cent of the patients

¹Read before the Radiological Society of North America, at the Twentieth Annual Meeting, at Memphis, Tenn., Dec. 3-7, 1934.



Fig. 2. Larynx from which specimen in Figure 1 was taken. Aryepiglottic fold, as well as the epiglottis, shows induration and thickening. Moderate amount of induration in the cuneiform and arytenoid cartilages. Ventricular illumination fairly normal. Both cords and bands can be clearly visualized.



Fig. 3. Complete disappearance of the tumor. Normal laryngeal illumination and structural relation.

they had treated by the x-ray had remained well for periods varying from six months to a year.

Other reports from Coutard have appeared during the past four years. Most of the cases treated were advanced and inoperable, and a goodly number of them were recurrences after surgery, many with metastasis to the cervical glands. Of 77 larynx cases, there were 25 survivals for three years (32 per cent), and of 89 pharyngeal cases, 14 (15 per cent) were alive and well after three years. This is by far the best result ever achieved in the radiotherapy of this particular lesion. A report on the same series made in 1934 revealed that 22 (28 per cent) of the laryngeal cases still survived, and 11 (12 per cent) of the hypopharyngeal cases. In both types of the disease there were survivals for more than seven years.

Stewart-Harrison treated a total of 116

cases, of which 105 were pharyngeal carcinoma and 11 carcinoma of the larynx. In 1932 he reported the results after three and a half years. "Local success" had been attained in 57 pharyngeal cases (54.2 per cent), and 34, or 32.3 per cent, were clinically free from malignancy at the time the report was made. Of the patients with carcinoma of the larynx, seven out of eleven showed the immediate success of the therapy, while six, or 54.5 per cent, were symptom-free when reported, from nine months to three and a half years later. Stewart-Harrison concludes: "The results of protracted fractional x-ray therapy in the treatment of cancer of the larynx and pharynx are not inferior, and are often superior, to those obtained by any other treatment."

Nager, Schinz, and Zuppinger, in 1934, presented their five-year results after using the method of protracted fractional dosage.

In a series of 121 cases of very advanced and inoperable carcinomas of the pharynx and hypopharynx, they obtained success in 25 (20 per cent), while from 10 intrinsic cases, four (40 per cent) had been symptom-free for from two to five years. These authors believe that in small, localized, intrinsic tumors, roentgen therapy alone can produce primary regression of the lesion, and lasting results in a large percentage of cases.

Lambadarides, between 1925 and 1933, treated 12 cases of laryngeal cancer, all advanced and inoperable. When the report was made, six were alive and clinically free of all indications of malignancy. Of these, one has survived nine years; one, six years; one, five years; one, three years; one, two years, and one for one year.

This author attributes the good results principally to the employment of the fractional protracted radiation, but points out that such factors as natural resistance, the precise location of the tumor, and, to a certain extent, the histologic structure of the lesion play a part in the prognosis. As all of these patients would have died quickly without the assistance afforded them by x-ray therapy, he considers his results most encouraging.

RESULTS OF SURGERY

It is instructive to compare the above results with those obtained by laryngeal surgeons. It is generally conceded that in cancers arising from the vocal cords, the symptoms are manifested early, and the disease progresses very slowly. It is held, therefore, that surgery can produce permanent results in intrinsic cancer of the larynx. But in extrinsic cancer the onset is insidious, and invasion of the lymphatics takes place early also. Since, therefore, surgery offers very little hope for extrinsic cancer, the majority of cases coming to the radiologist are of this type—inoperable from the outset.

The surgeon selects his cases, and must take into consideration not only the eradication of the disease, but the preservation of the voice, as well. The radiologist, deal-

ing with the most advanced and inoperable cases, has succeeded in preserving the voice in all his cases, and has eradicated the disease to the extent of being able to show patients who have remained well for periods as long as eight and nine years. These facts should be kept in mind, in order to make a fair comparison between the results of surgery and of radiation.

Chevalier Jackson (1934) reports results of laryngofissure in early laryngeal cancer, as follows: Forty-one cases (55 per cent) alive and well after five or more years; nineteen cases untraced after the first year; three died within five years of intercurrent disease; two died of cancer of other regions without local recurrence; nine died of recurrence in less than five years.

From these results, Jackson claims 82 per cent of survivals for five years or more.

St. Clair Thomson (1928), also performing laryngofissure in early intrinsic cases, reports 70 operations, giving survival rates as follows: Thirty-four (45 per cent) alive and well for three years or more; eighteen died of intercurrent disease, having been free from cancer for three years or more; seven died of distant metastasis; eleven died of local recurrence, eight of these within one year; three died of recurrence after three years; three died as the result of the operation.

On the basis of the above, Thomson gives 76 per cent as the average of lasting cures.

New and Waugh (1934), of the Mayo Clinic, stressing the importance of early diagnosis, give the following results in 107 cases, in which the patients underwent thyrotomy or laryngectomy: Sixty-nine (64.5 per cent) were alive and well for five years or more after the operation. They also point out that of the six microscopically Grade 4 tumors, which they were able to trace, not one survived the five-year period.

Cetra, reporting 149 laryngectomies, gives the following figures: Thirty-seven (24 per cent) survived for three years or more; seventeen (11 per cent) lived for three years; nine (6 per cent) lived for four



A.—Indirect mirror laryngoscopy showing the tumor mass involving arytenoid region and epiglottis at the beginning of roentgen therapy.



B.—Four weeks following roentgen therapy, showing the typical radio-epithelitis of the larynx and hypopharynx.



C.—At six weeks, definite regression of tumor mass.



D.—At eight weeks, continued regression of tumor mass.



E.—At fourteen weeks, moderate amount of edema of the arytenoid region. The cords can now be well visualized and function normally.



F.—At 66 weeks, complete disappearance of the tumor and restoration of the larynx to normal.

Fig. 4. Regressive changes in laryngeal cancer under roentgen therapy.

years, and eleven (7 per cent) lived for five years. In 46 cases there was adenopathy, but in some the histologic examination failed to reveal cancer tissue.

of surgery in both intrinsic and extrinsic carcinoma of the larynx, as follows: In ten cases of early intrinsic carcinoma, the tumor being confined to the cord

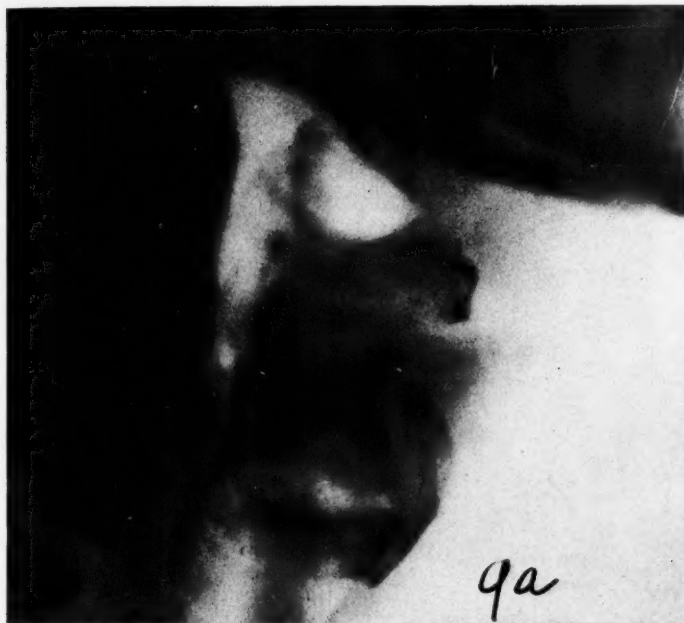


Fig. 5. Infiltration of the aryepiglottic folds and erosion of the epiglottic cartilages. Infiltration in the posterior wall of the larynx and thyro-hyoid tissues. The hyoid bone is displaced upward. Laryngeal vestibule is encroached upon by the tumor mass. Laryngeal illumination is diminished.

The results of surgery in laryngeal cases are given by Nager, Schinz, and Zuppinger, of the Zürich Clinic. Some of their patients likewise received post-operative roentgen therapy by the old method of massive dosage.

There were 280 cases treated in all, of which 23 growths were intrinsic and 257 extrinsic. Eleven patients (5 per cent) survived from one to nine years. Of the six patients with intrinsic neoplasms who were among these survivors, two had received post-operative roentgen therapy. Of the remaining five patients who survived, the growths had been extrinsic, and of these two received post-operative radiation with x-ray and two (sarcomas) were treated with radium.

Fielding O. Lewis (1931) gives the results

and laryngofissure being the operation of choice, four (40 per cent) survived five years or more. In advanced intrinsic carcinoma, laryngectomy was performed in 83 cases. Of these, 32 (38 per cent) survived five years or more. In extrinsic carcinoma of the larynx, with cervical metastasis, out of 75 cases operated on, 16 (21 per cent) were alive and well after five years.

Taking the entire group of 168 cases in which surgery was the method of treatment, 52 (30 per cent) remained alive five years or more. This operator favors pre-operative and post-operative radiation in the advanced intrinsic and extrinsic cases.

Colledge and Peacock (1932) report the results of surgery in 108 cases of intrinsic and extrinsic laryngeal carcinoma; 56 out of 60 were operated upon, either by total

laryngectomy (42), partial laryngectomy (3), or laryngofissure (11). These authors claim 80 per cent survival in the cases in which thyrotomy was performed. The

cases, 30 being intrinsic and 82 extrinsic carcinomas of the larynx, wherein surgery was carried out. Twenty-five (22 per cent) survived, 20 of these survivors having been



Fig. 6. Same case as shown in Figure 5, showing normal roentgenographic appearance of larynx following roentgen therapy.

time of survival is not definitely stated. Eleven (24 per cent) survived laryngectomy for three years or longer.

In the group of extrinsic cancers there were 48 cases: 24 were too advanced for surgery; one patient refused operation; pharyngotomy was performed in 23 instances. Nine patients (39 per cent) died as a direct result of the operation. Of the 14 surviving, eight lived for periods of from less than one year to two and one-half years, but eventually succumbed to the disease.

Orton (1932) operated on a series of 112

intrinsic cases. The time of survival is not given. Of the surviving five extrinsic cases, one has been alive and well for two years; one is alive, but with recurrence, and three are too recent to be reported as final results.

It is apparent, therefore, that conservative surgery as practised by Jackson, Thomson, New, and Clerf gives excellent results, but is applicable only to the very early intrinsic or cordal tumors, and in *selected cases*. Even in these, the results obtained are not without functional and physiologic disturbances of the larynx.

Jackson admits that only about 19 per cent of the cases which come into his hands are suitable for this kind of surgery.

When the disease has become extrinsic, radical surgery is necessarily mutilating, the patient is permanently disabled, and the consideration of the final results shows that the treatment is not warranted or justified. On the other hand, some surgeons report improved statistics in the results of operative treatment, when surgery has been combined with external radiation.

SOME FEATURES OF DIAGNOSIS

From the point of view of diagnosis, prognosis, and treatment, it is important to establish accurately the location of the laryngeal growth.

Direct and Indirect Laryngoscopy.—Neither direct nor indirect laryngoscopy can give fully information as to the extent of the disease, and in the mirror a carcinomatous area always appears smaller than it really is; but if x-ray examination and laryngoscopy are combined, a more accurate picture of the disease is obtained.

X-ray Examination.—The careful study and interpretation of roentgenograms will supply many data which will prove most valuable in guiding the therapist in the selection of the method of treatment to be adopted. X-ray examination not only supplies information as to the extent of the neoplastic invasion, but also reveals much as to the spread of the disease into the prevertebral pharyngo-epiglottic space, the subglottic and hyoid regions, as well as into the soft tissues. The roentgen examination likewise shows the extent of involvement of the laryngeal cartilages.

The roentgen examination may be made fluoroscopically or radiographically, or both methods may be employed. The fluoroscopic examination permits a preliminary general survey, and also a study of the mobility of the structures during phonation, deglutition, and respiration, while the routine roentgen examination provides the permanent record.

The alterations in the larynx and ad-

jacent parts produced by an intrinsic or extrinsic malignant neoplasm are visualized in the roentgenogram as erosion, infiltration, and displacement of both larynx and neighboring structures, as well as by obliteration or encroachment on the illuminated pharyngo-laryngeal spaces.

While treatment is in progress, and after its completion, roentgen examination gives information as to the reaction of the tissues to irradiation, and aids in determination of the dosage. After the treatment has been concluded, the x-ray examination permits the study of the progress of regression, and the detection of early metastasis or recurrence.

Biopsy.—The question of the wisdom of performing biopsies has long been a subject of lively discussion among those interested in the treatment of cancer of the larynx. Thomson thinks the clinical examination is far more important, and that many of the specimens taken are not large enough; also, at times, that the tissue may be, not only insufficient, but removed from the wrong place. Tucker, on the other hand, strongly advocates biopsy, regarding it as the conclusive diagnostic step in every case. He advises the use of the Jackson laryngoscope, for when this is employed a specimen from any desired site can be obtained promptly and accurately. Clerf believes that the factor of biopsy as an influence in promoting metastasis is largely theoretical, although he recognizes the possibilities of trauma at the time the laryngoscopy is done, and that to permit a long interval to elapse between taking the specimen and instituting treatment favors dissemination of cancer cells. Therefore, trauma and delay should be avoided.

RADIOSENSITIVITY

Although, generally speaking, the histologic examination and the grading of tumors provides valuable information, it must be stressed that there are numerous other factors which play an important rôle in the "radiosensitivity" or "radio-curability" of the individual tumor. Success in treatment depends upon the care-

TABLE I.—CLASSIFICATION AND RESULTS IN THE ROENTGEN TREATMENT OF 13 CASES OF LARYNGEAL CARCINOMA

Name Age	Symptoms— Duration	Location of Lesion	Cervical Glands	Type of Lesion	Histology	Dose and Time of Treatment	LIVING	
							Immediate Result	Final Result
1. H. Z. 48	Hoarseness—15 mos.	Ant. commissure and ant. half r. cord	Not palpable	Intrinsic	Squamous-cell ca., with hornification	8,620 r (33 days)	Complete regression of tumor; voice normal; chink wide	Alive and well (44 months)
2. J. P. 67	Hoarseness, 1 yr.; dyspnea, 3 weeks	Tumor involving almost entire cord and partially obstructing laryngeal vestibule	Not palpable	Intrinsic (advanced)	Squamous-cell ca., with little and incomplete hornification	6,700 r (24 days)	Complete regression of mass; voice normal; chink wide	Alive and well (44 months)
3. A. S. 33	Hoarseness, dysphagia, Rad. pain to head 6 mos. Continued hoarseness and trachea. (July 15, 1931)	Large mass filling lar. int. and extending to pyriform sinus and folds. Continued obstruction of larynx and partial obstruction of phar. vestibule. Tracheotomy	Palpable on l. side	Extrinsic	Squamous-cell ca.	5,040 r (23 days)	Rapid and progressive regression of tumor; removal of tracheal cannula and cessation of tracheostomy; alleviation of symptoms; chink and voice normal	Alive and well (39 months)
4. B. B. 65	Hoarseness and dysphagia	Ulcer and infected tumor mass in r. laryngeal vest., r. arytenoid, r. aryepiglottic fold, r. vent. band	Right cervical palpable	Extrinsic	Squamous-cell ca., with little hornification	8,400 r (27 days)	Rapid and progressive regression of tumor, with alleviation of symptoms; voice normal; chink wide	Alive and well (36 months)
5. F. F. 60	Hoarseness, dysphagia—6 months	Ulcer and infected tumor base epiglottis, folds r. band and pyriform sinus, arytenoid. Cartilage invasion	Palpable on r. side	Extrinsic	Squamous-cell ca., markedly anaplastic	8,064 r (28 days)	Rapid regression of tumor; mobility of cords re-established	Alive and well (24 months); complete regression of tumor and adenopathy
DEAD								
6. M. M. 55	Hoarseness—5 mos. dysphagia—2 mos.	Tumor mass involving r. lar. vest., r. vent. band, r. cord, post. half, and r. ventricle. Infiltration of pyriform sinus and post. cervical region	Not palpable	Extrinsic	Papillary ca., with pearl formation	9,900 r (48 days); treatment interrupted	Incomplete regression of tumor and presence of edema after first series of treatment; complete regression of tumor and edema after second series; voice normal; chink wide	Clinically well (36 months); recurrence—tracheotomy infection, and laryngeal necrosis, died
7. H. E. 68	Hoarseness, dysphagia, and dysphonia 2 mos.	L. valcule, l. glosso-epiglottic fold, l. pyriform sinus, epiglottis. Cartilage invasion of thyroid and epiglottis	Palpable on l. side	Extrinsic (advanced)	Squamous-cell ca.	8,250 r (17 days)	Incomplete regression of infiltrating and ulcerating mass; persistence of laryngeal edema; improvement of symptoms (5 mos.); recurrence and necrosis of cartilages	Died 14 months after treatment
8. M. W. 48	Hoarseness, dysphagia—2 yrs.	Ant. commissure, r. half base epiglottis, r. cord, r. vent. band; induration in pretracheal space	Both submax. glands enlarged	Intrinsic (advanced)	Squamous-cell ca., with hornification	8,500 r (19 days)	Eventual regression of infiltrating tumor but persistence of laryngeal edema; symptoms improved, lasting 10 weeks; laryngeal edema increased and tracheotomy	Died one year after treatment; autopsy, laryngeal cancer, and no evidence of carcinoma

9.	E. T. 58	Hoarseness, dysphagia, dyspnea, pain in l. ear—6 mos.	Epig. l. valcule, l. gl.-epigl. fold, base of tongue and l. pyriform sinus. Induration in prevertebral space	Bilateral	Extrinsic (advanced)	Squamous-cell carcinoma with hornification	8,470 r (26 days)	Regression and arrest of tumor growth with alleviation of symptoms and improvement of general condition (about 4 1/2 mos.); recurrence of symptoms and edema; tracheotomy	Died 10 months after treatment
10.	A. D. 72	Dysphagia and hoarseness—9 wks.; pain l. ear—3 wks.	Tumor of l. pyriform sinus, phar. and lar. wall; l. aryepigl. fold and band. Mobility of l. cord impaired. Edema of epiglottis	Not palpable	Extrinsic	Squamous-cell carcinoma	6,400 r (24 days)	Complete regression of tumor and alleviation of symptoms, lasting 7 mos.; gradual recurrence of dysphagia and laryngeal edema; tracheotomy	Well, 7 months, then recurrence; tracheotomy in April, 1932; untraceable
11.	J. B. 70	Hoarseness—5 wks.	Tumor located on ant. part of right cord	Not palpable	Intrinsic	Papillary squamous cell; numerous mitoses and anaplasia	9,300 r (52 days); treatment interrupted	Slow regression of tumor but persistence of laryngeal edema which eventually caused laryngeal obstruction and asphyxia; gastrostomy (tenth week); sloughing of tracheotomy wound and evidence of cartilage necrosis	Died 4 months after treatment, cardio-vascular disease
12.	A. C. 48	Dysphagia, hoarseness	Ulcer and infecting tumor mass involving epig. larynx, pyriform sinus, chink narrowed; tracheal cartilages in situ	Bilateral palpable cervical	Extrinsic (advanced)	Squamous-cell carcinoma with hornification	8,400 r (28 days)	Incomplete regression of tumor and arrest of progress of growth with alleviation of symptoms of pain and dysphagia for 3 months	Improved for 3 months; recurrence, alive with recurrence and pain after 8 mos. after treatment
13.	H. B. 42	Hoarseness, dysphagia—3 mos. Lar. pain and rad. pain to l. ear—2 mos.	Ulcer, and infecting tumor mass involving r. side epig., r. band and r. aryl. r. vent. Mobility of r. cord impaired. Tracheotomy.	Palpable deep and superficial chain involved	Extrinsic	Squamous-cell carcinoma with hornification	7,680 r (28 days)	Regression of tumor and edema of r. side; chink widened; tracheal cartilages removed; eventuality of spread and involvement of l. larynx and hypopharynx	Died with recurrence, metastasis, and involvement of l. deep and superficial cartilages and bronchial structures 6 months after treatment

ful consideration of many factors, such as the extent of regional metastasis, the size and location of the primary tumor, the amount of involvement of the cartilages, the presence or absence of secondary infection, the condition of the vasculo-connective tissue about the growth (tumor bed), the technical or physical factors in the treatment (time-intensity factor, etc.), and the patient's general physical state. These factors are as important as the histologic structure of the tumor, upon which so much stress is commonly placed.

Our conceptions of what constitutes radiosensitivity, or radioresistance in tumors, have recently undergone considerable modification. While histologic grading is undoubtedly very useful, work such as Coutard's, Schinz's, and Zuppinger's, and our own clinical experience, have definitely demonstrated that laryngeal growths (histologically squamous-cell epithelioma with hornification, which is usually found on the true vocal cord, and long considered to be highly radioresistant) can be made to yield readily to roentgen therapy, if the energy is distributed in relatively low intensities, and the treatment protracted over a long period of time. Indeed, after consideration of all factors known to play a rôle in radiosensitivity, we still cannot predict precisely how any given tumor will behave under irradiation.

TRACHEOTOMY

In our experience, tracheotomy has never been necessary during the course of treatment. If the chink of the glottis is

much narrowed, so that when the patient first comes under observation dyspnea is marked, or there is edema of the soft tissues, tracheotomy should be done before treatment is instituted.

This does not mean, however, that tracheotomy should be done as a routine, but, rather, the contrary. Only when edema and congestion of the mucous membrane seem likely to threaten asphyxiation is it necessary, but the decision must be made *before* the radiation is undertaken.

In laryngeal tumors, especially if they are subglottic, a low incision, opposite the second and third tracheal rings, will be found best. If the lesion lies below the glottis, there is danger when making the incision of cutting into the tumor itself, and opening up an avenue for infection and the spread of the disease.

When the patient has been tracheotomized before irradiation is instituted, the cannula should be removed before each treatment, and afterward replaced. This is important, because if it is left in place during treatment, the secondary radiation from the metal tube will cause marked local reaction, and may produce necrosis of the cartilage.

RADIO-BIOLOGIC PRINCIPLES

The principles underlying the modern concept of the technic of roentgen therapy are based on considerable biologic experimentation (Regaud and Blanc, Regaud and Nogier, Regaud and Ferroux, Schinz and Slotopolsky, Lacassagne), and practical clinical research (Coutard, Pfahler, Schinz, Berven, Zuppinger, Hirsch). It has been demonstrated beyond question that greater differential effects can be produced, as between the tumor cells and the cells of the adjacent and surrounding tissues, by the administration of radiation at a slow rate. Consequently, the desired biologic reaction in the tumor and normal tissues depends not only on the total energy delivered, but also on the rate (intensity/min.) at which it is delivered to the tissues.

By delivering the radiation at a relatively slow rate it is possible to give large

doses of hard rays, and to produce destruction of the epithelium of the skin and mucous membrane and reactive changes in the vasculo-connective tissues (tumor bed), with complete restitution of the normal tissues—a reversible reaction—while the effect on the neoplastic cells is permanent—irreversible.

Before considering the technic of the irradiation it is important to emphasize that though there are definite general principles underlying this treatment, each case is more or less an exception to the general rule. Success depends on the careful daily examination of the larynx during the treatment. The reaction of the normal mucous membrane of the larynx, as well as the response on the tumor tissue, permits modification of routine which each particular case seems to demand.

TECHNIC OF IRRADIATION

Though the treatment by the x-ray would seem to be a relatively simple matter, experience has shown that malignant growths in this particular region present many technical problems; so that even partial success can be attained only by the most scrupulous attention to every detail.

We use two constant potential, kenotron rectification power plants. One is a Wappler Quadrocondex machine and the other a Stabilivolt apparatus. The tubes are the Philips Metalix water-syphon cooling type, overhead suspension. The voltage used is 180 K.V.; 4 ma.; 60 cm. skin-target distance; 2 mm. copper plus 1 mm. aluminum filtration. The half value is 1.85 copper, the effective wave length (λ eff.) is 0.11 Å. The depth dose (10 cm.) is 36 per cent and the intensity is 6.4 r per minute on the surface.

Fields of Irradiation.—It is necessary to irradiate not only the local lesion but the regional lymphatic basin as well, even though no adenopathy is present. Accordingly, the portals are somewhat larger than those usually utilized, averaging between 100 and 125 square centimeters.

The portals comprise the right and left

cervical areas. The boundaries of the fields are the clavicle below, and the lower border of the ramus of the mandible above; the median line of the thyroid in front, and the posterior border of the sternomastoid muscle posteriorly.

Dosage.—The mucous membrane reaction—both the time of its appearance and its intensity—may be used as a biologic control of the dose.

A good reaction of the mucous membrane appears to be associated with a satisfactory regression of the tumor. A too rapid completion of the total dose, or a too large daily dose, may result in permanent destruction of the vascular connective tissue with cartilage necrosis, incomplete sterilization of the neoplasm, laryngeal edema, and rapid recurrence.

In the cases in which good results were obtained, the total dose varied from 5,000 r on the surface, given over a period of 23 days, to a maximum of 8,600 r in 33 days. Treatments are given daily, six times a week. In the cases that have died the dosage varied between 6,400 r in 24 days to a maximum of 9,900 r in 48 days.

The criteria for sufficient dosage is the evidence of complete destruction of the mucous membrane of the laryngo-pharynx or, as commonly known, a homogeneous radio-epithelitis.

When because of syphilis, diabetes, arterio-sclerosis, or chronic cardio-renal disease, the mucous membrane reaction is atypical, the reaction of the epidermis of the skin is the guide. Dosage sufficient to produce complete exfoliation is administered.

CLINICAL MATERIAL

Our material consists of 13 cases of histologically proven laryngeal carcinoma, treated between 1929 and 1932. All the patients were men. The youngest was 35 and the oldest 72 years of age.

From the histologic point of view, all lesions were squamous-cell carcinoma. Nine showed various degrees of hornification; two showed anaplasia, and in the remaining

TABLE II.—ANALYSIS OF CASES

	Histology—Squamous-cell Epithelioma					
	In-trin-sic	Ex-trin-sic	Glands Pal-pable	Hornification	Anaplasia	No Hornification
Alive (5)	2	3	3	4	1	0
Dead (8)	2	6	5	5	1	2
Total (13)	4	9	8	9	2	2

Ages of patients: 35 to 72 years
Sex: all males
Most common symptoms: hoarseness, dysphagia

TABLE III.—RESULTS

	Total	Alive and Well 24-44 months	Dead
Extrinsic	9	3 (33%)	6
Intrinsic	4	2 (50%)	2
Total	13	5 (38%)	8

two there was no evidence of hornification or pearl formation.

The most common symptoms were hoarseness and dysphagia.

There was definite cervical adenopathy in eight cases. The adenopathy usually corresponded to the side of the lesion. The very advanced cases presented bilateral cervical adenopathy, and the superficial, as well as the deep cervical, chain of glands were involved.

In three cases, before treatment was given, tracheotomy had to be performed as an emergency procedure, to prevent death by asphyxia. One of these patients is now alive and has been well for three and one-half years.

There were four intrinsic and nine extrinsic cases. Even in the intrinsic lesions, the involvement and anatomical location were such that they were not suitable for conservative surgery (thyrotomy).

In all, definite regressive changes took place and in practically all, the tumor primarily disappeared.

Eight patients have died. Two of these were intrinsic, and six extrinsic cases. One of these patients lived three years in comfort, and was free of the disease. Recur-

rence, with ulceration and infection and adenopathy, then took place. The patient was retreated, but laryngeal edema set in and tracheotomy had to be performed. This patient subsequently died of general sepsis and cartilage necrosis. In the other fatal cases recurrences were observed between the fifth and twelfth months. In one death from laryngeal edema, permission was obtained to remove the larynx and a careful histologic examination was made of the entire organ. There was no evidence of carcinoma in any of the sections.

Of the five patients alive and well, two cases are intrinsic and three extrinsic. From the clinical and histologic points of view the prognosis in these cases was unfavorable, because of the extension of the disease, cervical adenopathy, and the microscopic finding of hornification and pearl formation.

Two patients are alive and well with no clinical evidence of disease, and have good function of the larynx after forty-four months. One case was retreated after eighteen months, because of suggestive symptoms of reactivity (slight dysphagia, moderate edema of the arytenoid region). All these symptoms have cleared up following the second series of roentgen treatment. The patient is now alive and well, twenty-four months since the initial series of treatment.

SUMMARY

The roentgen examination is a valuable aid and guide in the diagnosis and treatment. It aids laryngoscopy in giving an accurate picture of the disease.

Biopsy, when followed by treatment within a reasonable period of time, does not predispose to metastases.

Tracheotomy is a life-saving procedure in advanced cases with total obstruction of the larynx, and should in selected cases be done before instituting treatment. Routine tracheotomy, in cases in which there is no evidence of marked laryngeal obstruction is not indicated.

The failure to obtain a clinical cure appears to have been due to several factors:

1. The nature of the lesion. The advanced and unfavorable condition of the case, with involvement of the deeper structures of the larynx, muscles, perichondrium, cartilages, and superimposed infection—all these factors acting in such a way as to make it impossible to obtain more than temporary alleviation.

2. Faulty technic.

3. Systemic state.

General debilitating diseases, old age, cardio-renal disease—contribute to the production of an atypical mucous membrane and skin reactions and thus complicate the estimation of the proper dosage.

CONCLUSIONS

On the basis of analysis of the literature on the results of the evaluation of the surgical and roentgen treatment of laryngeal cancer, as well as the study of 13 cases of our own, it may be stated that—

1. In intrinsic cases clinical cures can be obtained by roentgen treatment in cordal, glottic or subglottic, non-infiltrating, keratinizing, fully differentiated squamous-cell epitheliomas. In such cases surgery gives equally good results, but with a lesser degree of conservation of function and with an average operative mortality of about 15 per cent.

2. In the extrinsic cases in which the tumor involves the epiglottis, glosso-epiglottic folds, valleculæ, pyriform sinus, hypo- and lateral pharyngeal and post-cricoid regions the prognosis is usually unfavorable due to the tendency to rapid spread and metastatic glandular involvement. In this group surgery gives a high mortality and offers no assurance of cure. Roentgen therapy can produce a clinical cure in this group with cervical involvement, or, if the case is hopelessly advanced, palliation, comfort, and prolongation of life.

REFERENCES

- BERVEN, E.: *Acta Radiologica* (suppl.), 11, 1.
 CETRA, C. M.: *Bol. Inst. de med. exper. para et estud. y trat. del cancer*, 1933, 10, 564.
 CLERF, L. H.: *Arch. Otolaryngol.*, 1934, 19, 653.
 COLLEDGE, L., and PEACOCK, R.: *Jour. Laryngol. and Otol.*, 1932, 47, 161.

- COUTARD, H.: *Am. Jour. Roentgenol. and Rad. Ther.*, 1932, **28**, 313.
IDEM: *The Lancet*, July 7, 1934, p. 1.
IDEM: Band II, *Referata, Internationaler Radiologen Kongress, Zürich*, 1934, p. 87.
COUTARD, H., and HAUTANT, A.: *Ann. Mal. Oreille*, 1923, **42**, 962.
GUNSETT, A.: *Röntgenpraxis*, 1932, **4**, 214.
HIRSCH, I. S.: *The Principles and Practice of Roentgen Therapy*.
HIRSCH, I. S., and BAUM, S. M.: *Laryngoscope*, February, 1934.
JACKSON, C.: *Surg., Gynec. and Obst.*, 1934, **58**, 431.
LACASSAGNE, A.: *Radiophys. et Radiother.*, 1930, **1**, 401.
LAMBADARIDES, A.: Band II, *Referata, Internat. Radiol. Kongress*, 1934, p. 379.
LENZ, M., COAKLEY, G. C., and STOUT, A. P.: *Am. Jour. Roentgenol. and Rad. Ther.*, 1934, **32**, 500.
LEWIS, F. O.: *Trans. 37th ann. meeting Am. Laryngol., Rhinol., and Otological Soc.*, 1931, pp. 326-330.
MONOD, O.: *Radiophys. et Radiother.*, 1928, **1**, 207.
NAGER, F. R., SCHINZ, H. R., and ZUPPINGER, A.: *Schweiz. med. Wchnschr.*, 1934, **29**, 695.
NEW, G. B., and WAUGH, J. M.: *Surg., Gynec. and Obst.*, 1934, **58**, 841.
ORTON, H. B.: *Jour. Am. Med. Assn.*, Jan. 23, 1932, p. 290.
PARÈS: *Jour. de radiol. et d'electrol.*, October, 1922, **6**, 467, 468.
PFAHLER, G. E.: *Surg., Gynec. and Obst.*, 1925, **41**, 443.
REGAUD, C.: *Radiophys. et Radiother.*, 1930, **1**, 443.
IDEM: *Acta Radiologica*, 1930, **11**, 455.
REGAUD, C., and BLANC: *Compt. rend. Soc. de Biol.*, 1906, p. 61.
REGAUD, C., and NOGIER: *Compt. rend. Acad. d. Sc.*, 1914, **158**, 1711.
REGAUD, C., and FERROUX: *Strahlentherapie*, 1929, **31**, 495.
SCHINZ, H. R., and SLOPOLSKY: *Ergebnisse der med. Strahlenforschung*, 1925, **1**, 443.
STEWART-HARRISON, R.: *Laryngol. and Otol.*, 1932, **47**, 721.
THOMSON, ST. CLAIR: *Arch. Otolaryngol.*, October, 1928, **8**, 377-385.
TUCKER, G.: *Ann. Otol., Rhin., and Laryng.*, March, 1932, **41**, 36-51.
ZUPPINGER, A.: *Ztschr. f. Hals-Nasen u. Ohrenh.*, August, 1931, **28**, 514-531.

DISCUSSION OF SYMPOSIUM ON MOUTH AND NECK¹

Dr. MAX CUTLER (Chicago): I appreciate the privilege of discussing Dr. Meland's paper. The prognosis of intra-oral carcinoma is dependent upon two factors: the extent of the disease and the histologic structure. The question of prophylactic radiation in the absence of clinical evidence of disease in the neck I think constitutes an extremely difficult problem. My present feeling is against using any form of prophylactic radiation for the cervical area when there are glands to be found on clinical examination.

In that respect I agree with the principles of the French school, taking the position that when prophylactic irradiation is administered under these circumstances, the skin is so altered and injured that a subsequent complete adequate irradiation becomes impossible if or when lymph nodes subsequently appear. This reason, added to the well-known fact that metastases do often appear in the face of such prophylactic irradiation, has led me to adopt the procedure of not irradiating the neck, prophylactically in intra-oral cancer.

I use seeds in areas in the tongue that are difficult to treat by removable platinum needles, as, for example, at the base of the tongue. On the other hand, I have found no difficulty whatever in retaining removable platinum needles in place by suturing them. If each needle is sutured in place, there is no difficulty in retaining them in position.

I was exceedingly interested in the paper on carcinoma of the larynx. I believe there are three problems with which we are confronted at present in the treatment of carcinoma of the larynx: first is the group in which the lesion is limited to the vocal cord; second, the group in which the lesion has infiltrated beyond the cord but is essen-

tially an intrinsic lesion; third, extrinsic carcinoma of the larynx.

Concerning the last group, there is no difference of opinion amongst surgeons and radiologists that radiotherapy is the method of choice. So far as the first group is concerned—lesions limited to one vocal cord—I am convinced that if proper radiation facilities are available and the individual using them has had adequate experience in their use, protracted radiation according to the Coutard method constitutes the method of choice as the initial treatment.

The intermediate group of cases, or that group in which the lesion begins as an intrinsic carcinoma but soon infiltrates the muscles and cartilage, constitutes a very difficult problem at the present time. This is the group in which radiation, even by the Coutard method, has yielded a very small percentage of cures. There is a great question as to the therapeutic method of choice in this rather large group of cases because, once the muscles and cartilage are infiltrated, radiation has usually failed. My present attitude concerning the treatment of carcinoma of the larynx is to use protracted irradiation for localized carcinoma of the vocal cord, protracted radiation for extrinsic carcinoma of the larynx, but until we have further evidence, laryngectomy for intrinsic carcinoma of the larynx which has infiltrated the muscles or cartilages when no contra-indications to operation exist.

Concerning Dr. Garland's paper, Coutard is at present protracting his treatment over a longer period of time rather than diminishing the time of treatment. I think Dr. Garland is to be congratulated on his courage for persisting in the treatment of such an advanced group of cases. Even 16 per cent control is excellent in a group in which such a high proportion are advanced.

In my opinion the radiation has been administered too rapidly and through too large a field in Dr. Garland's cases. I understood that 32 r units were given per minute through a field 14×14 centimeters in thirty days. I think that this radiation is too intense. I would advise rather than shortening the time of irradiation that the

¹ The paper by George E. Pfahler, M.D., entitled "The Treatment of Epithelioma of the Cheek," was read by title and published in *RADIOLOGY*, January, 1935, 24, 99-109.

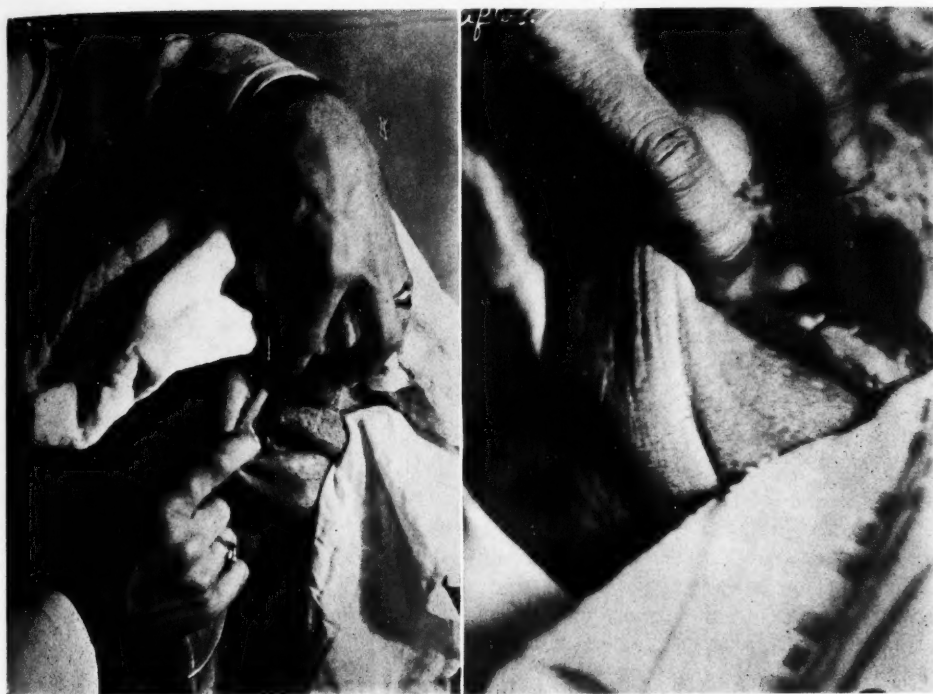


Fig. 1

time of irradiation be protracted and that the fields be reduced in size so that the intensity of treatment is diminished.

DR. JOHN S. DERR (Frederick, Maryland): I have one case I would like to report. It is a case of cancer of the tongue in a man 58 years of age. When he was first seen in 1929, there was a small growth far back on the side of the tongue. This was treated with electro-coagulation and low voltage x-rays through the neck and jaw. About three years later he returned with an increased growth. Dr. Merritt, of Washington, who saw him in consultation with me, inserted six radium needles around the mass. He received a heavy dose of high voltage x-rays through both sides of the neck before and after the radium treatment. Results in 1932 are shown in Figure 1. There has been no recurrence.

DR. ROBERT S. STONE (San Francisco): In connection with the Coutard method, I would like to ask the essayists in their

closing remarks to take up with us the point that Dr. Cutler introduced in his discussion about protracting to a greater period of time.

As I understand the commencement of Coutard's method, it was the result of Regaud's experiments on the testicles of rabbits. He decided that the proper time in which to treat these rabbits' testicles to get the best result was from four to nine days. Now, of course, the life cycles of tumor cells may be entirely different from the life cycle of the cells in the testicle of a rabbit. We do not know the length of the life cycle of any particular tumor and probably if we were able to determine that we would know better how long to treat these patients.

However, it seems to me, in watching these patients who are treated with the protracted fractionated dose, that if we give a good heavy dose they get their mucous membrane reaction in from ten days to two weeks.

A tumor that arises from the mucous membrane, it seems to me, would have somewhat the same type of life cycle as the mucous membrane from which it arises; if anything, somewhat shorter. Therefore, it would seem on hypothetical grounds that we should give the treatment in from ten days to two weeks instead of drawing it out to a matter of several months.

I may be mistaken but it is my understanding that Coutard's results since he has been protracting his treatment to a longer period are not so good as they were in the early days when he gave them in a shorter period of time.

Of course, the other problem is that we are dealing with a patient as well as a tumor, and it may be that the patients will be unable to stand the dose that would be administered in a shorter period of time. Watching these patients, however, both as regards the mucous membrane and as regards their skin, and seeing both surfaces react severely and then recover while you are continuing to administer daily doses of roentgen rays, makes one feel that the tumor can probably do exactly the same thing. While we are going on giving the radiation, the tumor may have recovered from its reaction and returned to its normal growth.

One other point I would like to bring up is the question of prophylactic radiation of the neck. I think that if we are going to do prophylactic radiation of the neck, we should not do it in any half-hearted way as if we are going to put a little radiation on there in the hope that it might stop a cancer coming. We have to treat the neck under the assumption that there is some cancer there, so microscopic we are unable to feel it. If there is none there, then Dr. Cutler is right—there is no point in giving radiation. If there is some there, then a mild dose applied to the neck is of no use whatever. We have to either give no radiation to the neck or we have to treat it as if we imagined a cancer there, and give it a full dose.

DR. O. N. MELAND (closing): I am glad

the question of prophylactic radiation has come up. As you remember, I told you I did not know how much good prophylactic irradiation did. However, I know this: That we have not controlled the malignancy in any of the neck cases by the ordinary methods of irradiation. We also know this: When we give 1,200 r and wait six or eight weeks, we are still able to do a neck dissection with primary healing.

If you are going to give your patient a full radiation dose under the assumption that you are dealing with a malignancy even though nothing is palpable, I doubt very much whether the patient will go through any surgical procedure in the line of a neck dissection.

I did not go into the matter of technic to any extent. You all know how to treat these patients. The only reason why I wanted to present the paper was to emphasize the necessity of having these patients sent to you when the lesion is small. If you take home nothing more than this, do take the necessity for treating patients when the lesions are curable.

It is up to us as consultants to go back to our general practitioners and to our dentists and urge them to institute a campaign on the necessity of biopsy in all doubtful cases in which there is a lesion involving the tongue or the internal surfaces of the mouth.

DR. BAUM (closing): We use somewhat larger fields than have been pointed out by Dr. Cutler: our average cervical area is about 100 square centimeters. We do this because we feel that even in the early cases in which no cervical metastatic glands are palpable, there is no such thing as being certain that cancer cells have not invaded the regional lymphatic drainage basin. The larger field will irradiate not only the local lesion, but the regional lymphatics as well. In advanced cases with definite unilateral or bilateral cervical glands we use larger fields—125 to 140 sq. cm.—irradiating the entire cervical area from one mandible to the clavicle. By protracting the treatments over a longer period of time—

40 to 50 days—we can give large dosages, resulting in complete exfoliation of the skin, but with complete restoration *ad integrum* in a period of a fortnight. We have seen definite metastatic glands regress completely under this form of treatment; and in spite of the large dosages some of the patients have received there is no telangiectasia or atrophy after observing some of these cases for over three years.

In reference to Dr. Meland's paper: we also use platinum needles in the anterior two-thirds of the tongue. In the posterior region of the tongue, however, we use removable platinum radon seeds filtered by 0.3 or 0.4 mm. of platinum. We prefer seeds because they can be deposited more accurately and because they can be more adequately held in place.

DR. L. H. GARLAND (closing): In answer to Dr. Cutler I may say that we use only large fields with extensive pharyngeal lesions. The fields vary in size in every case, one patient being treated with fields as small as 7×5 centimeters. The length of treatment in days also varies considerably; one of our cases was treated in 13 days, one in 80 days; the majority were finished in 36 days.

One of the Doctors asked me a question about the r per minute. This has usually been approximately 30. This is, of course, a marked departure from Coutard's technic; however, under circumstances in which it is necessary to treat many patients each day it would be almost impossible to use only 5 r per minute.

A RADIO FREQUENCY HIGH VOLTAGE APPARATUS FOR X-RAY THERAPY¹

By ROBERT S. STONE, M.D., M. STANLEY LIVINGSTON, PH.D., DAVID H. SLOAN,
M.S., and MILTON A. CHAFFEE, A.B., *San Francisco*

Division of Roentgenology of the Medical School and the Radiation Laboratory of the
Department of Physics, University of California²

PART II

IN THE previous issue of this Journal a radio frequency high voltage apparatus for x-ray therapy was described. The construction of the apparatus, as can be determined from the previous description, is such that the high voltages

complete absorption curve; (2) the "equivalent voltage" of Lauritsen; (3) the constant potential equivalent of Taylor; (4) the half value layer; (5) the effective wave length of Duane, and (6) the average wave length. The effective wave length and the average wave length methods are not used in the range of voltages here described.

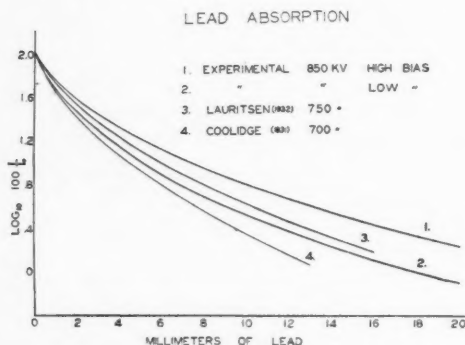


Fig. 7. Curves of absorption by lead.

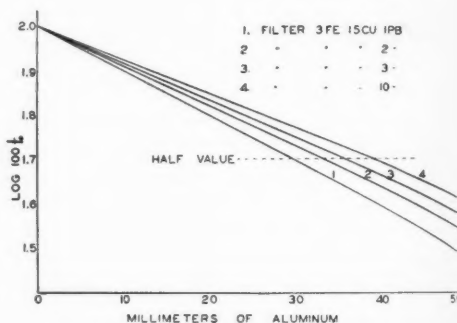


Fig. 8. Curves of absorption by aluminum.

are made and kept within a vacuum tank. Therefore, it is not possible to measure the peak voltages by the usual sphere gap method or by a voltmeter.

It is necessary, therefore, to state the quality of the radiation. The commonly adopted methods of specifying the quality of an x-ray beam are the following: (1) the

¹ Presented before the Radiological Society of North America at the Twentieth Annual Meeting, at Memphis, Tenn., Dec. 3-7, 1934.

² We wish to acknowledge the generous support of Mr. William H. Crocker, of San Francisco, which has made this installation possible. The Christine Breon Fund for Medical Research has contributed some of the funds for the investigations. The original development of the method was largely supported by the Chemical Foundation and the Research Corporation. The advice and assistance of Professor E. O. Lawrence, of the Physics Department, and Professor H. E. Rugles, of the Division of Roentgenology, have been of inestimable value.

Method of Obtaining Percentages of Absorption.—A lead diaphragm 2.5 cm. thick, with a circular aperture 2 cm. in diameter in its center, was placed just outside the wall of the tube at a distance of 42 cm. from the target. A second similar diaphragm was placed at the entrance to a lead cylinder 12 cm. in diameter and 60 cm. long. Thus a beam of rays could be directed down the axis of the lead cylinder so as not to touch its walls. An aluminum ionization chamber, 14 cm. long and 7 cm. in diameter, with walls 0.3 mm. thick, was placed at the far end of the lead cylinder. It was connected to a string electrometer (Fricke-Glasser dosimeter). The quantity of radiation was measured by the time taken for the indicator to pass over the complete scale.

The influence of scattered radiation from the room was largely eliminated by taking initial readings with the entrance to the

must be near the peak of the applied voltage. The effect of applying various grid-bias voltages on the shield of the

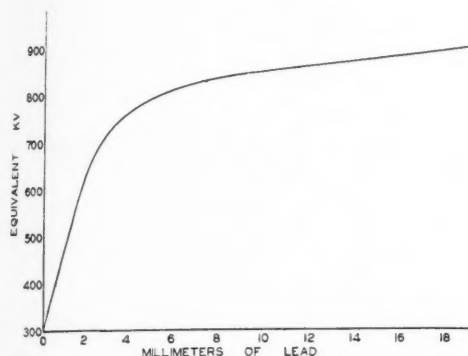


Fig. 9. Curve showing the increase of "equivalent voltage" with increase of lead filtration.

lead tube blocked by 10 cm. of lead. The wall of the tube consists of 0.5 mm. of copper plus 3 mm. of steel, both of which constitute a permanent initial filter.

Complete Absorption Curve.—Lead is the absorber usually used for obtaining curves up to nearly complete absorption in the high voltage range because the total thickness required need not be more than 2 centimeters. The physical data concerning the absorption in this metal are complicated by the photo-electric effect, whereas those for the lighter elements are not. Therefore, it is less convenient for the estimate of the equivalent voltages. Because the nearly complete curve is obtained so easily, however, such curves are valuable for comparing the performance of different x-ray tubes, and the operation of a given tube under different conditions. In general, the slope of the curve of the percentage of transmission becomes steeper for radiation produced by lower equivalent voltages.

The curves obtained are shown in Figure 7 along with those obtained by Lauritsen (2) and Coolidge (3). Their voltages were measured by direct methods. A comparison of the slopes of these curves after high filtration indicates that the equivalent voltage in our tube was 850 K.V. This

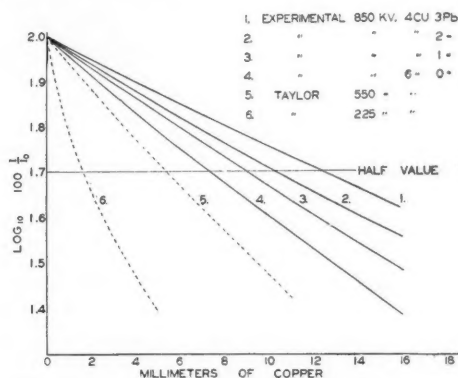


Fig. 10. Curves of absorption by copper.

cathode is shown clearly by the two experimental curves in this figure. After filtering through the first 10 mm. of lead, the remainder of each curve has nearly the same slope and, therefore, indicates the same voltage. The higher position of the curve with the higher grid-bias indicates a much greater percentage of transmission of the initial intensity. In other words, the initial radiation contains a much smaller proportion of long wave length radiation when the bias is so high, and the operation approaches that of constant potential applied voltage.

The slope and position of the curves after filtration through 1 mm. of lead show that while the difference in the percentage of transmission is small for the two different grid-bias voltages, the lower bias produces a lower equivalent voltage in addition to the slightly lower percentage of transmission. When the filtration of the lower biased curve is increased to 2.5 mm. in order to attain an equivalent voltage as great as that which the more strongly biased curve has after filtration through 1 mm. of lead, the percentage of transmission is only one-half as great as that for the stronger bias. This effect is much more pronounced when greater variations in the bias are used.

The effect of varying the grid-bias voltage, with a constant applied voltage and a constant emission current, is that an increase in the bias increases the intensity as well as the quality of the radiation. Increasing the filtration can raise the equivalent voltage and thus the quality of the radiation, but it does so with considerable sacrifice of intensity. This apparatus thus demonstrates the futility of specifying the quality of radiation in terms of the peak voltage. Using the same applied or peak voltage and the same filtration, the quality as well as the quantity of radiation can be changed at will by varying the bias applied around the cathode filament.

Equivalent Voltage from the Curve of Absorption in Aluminum.—The term "equivalent voltage" as applied to describing the quality of a composite beam of x-rays has been popularized by Lauritsen (4). He defined equivalent voltage as that required to produce radiation of equivalent wave length. "Equivalent wave length" is further described as that wave length of monochromatic radiation which has some pre-determined measurable property in common with the beam in question. A readily measurable property of any beam is its half value layer in different absorbers. In choosing the absorption material, certain properties are desired. Absorption by the collision of x-ray photons with electrons, called "Compton scattering" is described accurately by the Klein-Nishina formula. Aluminum, water, and the light elements have only this type of absorption for radiation in the range between 600 and 1,000 K.V. Absorption by the heavier elements is complicated by varying amounts of photo-electric absorption in addition to Compton scattering. For this reason, copper and lead absorbers are not well suited to determining the equivalent voltage.

The correctness of the Klein-Nishina formula for the absorption in the light elements, such as aluminum, has been verified by Lauritsen. The formula may be depended upon, therefore, to give the

correct equivalent voltage for radiation absorbed by any of the light elements. On this basis, Lauritsen (4) has plotted a very useful curve using the half value layer in water, to determine the equivalent voltages of any beam of radiation after any initial filtration. Leucutia and Corrigan (5) have added a similar curve using aluminum.

The curves of absorption in aluminum after varying initial filtrations, using the same applied voltage and the same grid-bias, are shown in Figure 8. The half value layer is obtained from this curve at 1.7 (*i.e.*, $\log_{10} 50 = 1.7$). By locating these half value layers on Lauritsen's calculated curves, the following equivalent voltages are shown:

1 mm. lead.....	460 K.V.
2 mm. lead.....	620 K.V.
3 mm. lead.....	710 K.V.

This increase in equivalent voltage with increase of initial filtration is represented graphically in Figure 9. The initial filtration in all cases is 0.5 mm. of copper plus 3 mm. of steel.

An estimate of the peak voltage can be obtained by using that thickness of lead which the curve of absorption in lead shows to produce an almost even slope, *i.e.*, more lead merely decreases the intensity without increasing the quality. Such a condition is present after about 1 cm. of lead filtration. The half value layer in aluminum after such a filtration is 39 mm., which indicates an equivalent voltage of 850 K.V., in this case nearly the peak voltage.

Constant Potential Equivalent.—The Committee on Standardization of X-ray Measurements of the Radiological Society of North America has recommended the use of the curve of complete absorption in copper, together with a statement of the initial filtration as a satisfactory method for stating the quality of the x-radiation. They agree that the statement of the equivalent constant potential, applied to the tube terminals to yield the same curve, may be used as a single numerical designation (6). Taylor and Singer (7) recently published curves of absorption in

copper for constant potential voltages up to 550 K.V. By "constant potential equivalent" they mean the constant po-

filters in addition (Fig. 10). The initial filter used was 3 mm. of steel plus 3.5 mm. of copper.

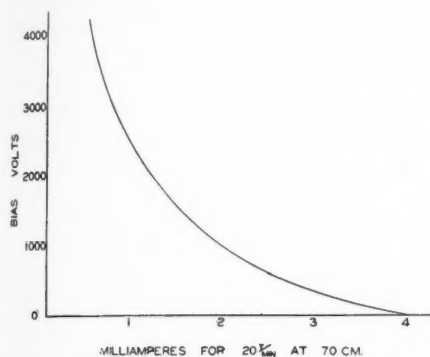


Fig. 11. Curve showing the number of milliamperes required to produce 20 r per minute with decreasing bias voltages.

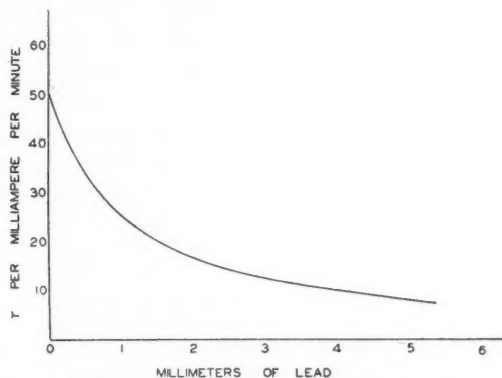


Fig. 12. Curve showing the r output per milliampere-minute with varying lead filters.

tential necessary to apply to an x-ray tube to yield a "simple" absorption curve of the same form as the composite absorption curve in the same material for the unknown radiation in question.

While copper may be an adequate absorber for voltages up to about 200 K.V., there are not sufficient data on the nature of the complex absorption in it for voltages above that level to permit the plotting of a useful curve or for obtaining the half value layer. Lead is a better heavy element for curves of complete absorption and aluminum is a better element for obtaining equivalent voltages, as has been shown above. The introduction of copper as an absorber for short wave length x-ray would seem to complicate the literature needlessly with data which could not be interpreted easily in terms of any other element. However, because roentgenologists are so accustomed to think in terms of the absorption in copper, and because Taylor and Singer have published standard curves made with constant potential currents up to 550 K.V., a curve was obtained, using as nearly as possible the same initial filter as theirs, and other curves using lead

Effect of Grid-bias Voltage.—Most, if not all, previous x-ray tubes have used the full high voltage of the tube on a shield of some type around the filament to focus the cathode stream. Few, if any, have used the principle, above described, of having a negative potential wall close to the filament so as to prevent the electrons from leaving the neighborhood of the filament until the higher ranges of potential difference between the cathode and anode are reached. By this means, only high speed electrons can reach the target, which is saved from bombardment and consequent production of heat by low speed electrons, and the resultant beam of x-rays contains a much higher proportion of the desired short wave rays.

The effect of varying the grid-bias on the r output per milliampere of emission current is well shown by the curve in Figure 11. The quantity output was kept constant at 20 r per minute at a distance of 70 cm. from the target. The r output was measured by means of a parallel aluminum plate ionization chamber of the open air type and a high sensitivity galvanometer. The filter consisted of the

following, in the order given: 0.5 cm. Cu, 3 mm. steel, 1 mm. Pb, 1 mm. Cu. The following readings are typical:

4 ma.....	no bias
2 ma.....	1,000 volt bias
1 ma.....	2,500 volt bias

Effect of Filters and Grid-bias on the r Output.—The quantity output of radiation as measured in r units per milliamper-minute is an important consideration in any apparatus. Hence the curve shown in Figure 12 is reproduced to show this factor for the apparatus under discussion.

In treating patients, a constant output of 20 r per minute has been used and thus curves are not given for excessively high outputs which could be used if desired.

SUMMARY

1. An apparatus is described which uses a radio frequency circuit to provide high voltages for the production of x-rays to be used therapeutically.

2. The apparatus is shown to be rugged, compact, and economical in construction and operation.

3. The curves of absorption in lead show a peak voltage of at least 850 K.V. The application of grid-bias voltages to a shield around the cathode filament results in operating characteristics simulating those of constant potential apparatus.

4. The "equivalent voltage" as determined by the curve of absorption in aluminum is shown to be high in proportion to the applied voltage. With an applied voltage of about 850 K.V., an equivalent voltage of 620 K.V. is attained with 2 mm. of lead, and 710 K.V. with 3 mm. of lead as a filter.

5. The "constant potential equivalent" is high, but this method of measurement of high voltages is not recommended.

6. The great advantage of a grid-bias voltage applied around the cathode filament is demonstrated by showing the reduced amount of emission current needed to get the same r output and a better quality of beam.

7. The r output per milliamper-minute is shown to be satisfactory.

REFERENCES

- (2) LAURITSEN, CHARLES C.: Personal communication. Our thanks are given for permission to publish this curve.
- (3) COOLIDGE, W. D., DEMPSTER, L. E., and TANIS, JR., H. E.: *Am. Jour. Roentgenol. and Rad. Ther.*, 1932, **27**, 405-414.
- (4) LAURITSEN, CHARLES C.: *Am. Jour. Roentgenol. and Rad. Ther.*, 1933, **30**, 380-387, and 529-532.
- (5) LEUCUTIA, T., and CORRIGAN, K. E.: *Am. Jour. Roentgenol. and Rad. Ther.*, May, 1934, **31**, 628-662.
- (6) Standardization Committee of the Radiological Society of North America, 1933 committee report, Paragraph 7.
- (7) TAYLOR, LAURISTON S., and SINGER, GEORGE: *Bureau of Standards Journal of Research*, April, 1934, **12**, 401-420.

THE DIAGNOSTIC AND THERAPEUTIC VALUE OF THE INTRATRACHEAL USE OF IODIZED OIL IN CASES OF INTRACTABLE ASTHMA

WITH SPECIAL REFERENCE TO ITS USE AS A CONTRAST MEDIUM AND THE PHYSICO-CHEMICAL MECHANISM ON WHICH ITS THERAPEUTIC VALUE IS BASED¹

By RAY M. BALYEAT, M.D., L. EVERETT SEYLER, M.D., and H. A. SHOEMAKER, PH.D., *Oklahoma City, Oklahoma*

THE treatment of all types of asthma by methods based on allergic findings has proved satisfactory in our hands in about 70 per cent of the cases; in the other 30 per cent, results have been only fair or poor. In a review of 1,240 asthmatic patients whom we have studied in our clinic during the past five years, we find that excellent or good results usually were obtained from those suffering from periodic attacks of asthma but who had periods during the year in which they were entirely free. On the other hand, fair or poor results were usually obtained in those patients who had periodic attacks of severe asthma but who also, daily between attacks, had either light attacks or raised considerable white glairy or semi-purulent mucus. Others working in the field of allergy have obtained somewhat similar results.

Anderson (1), in 1932, reported good results in several cases of a series of asthmatic patients to whom he had given iodized oil intratracheally as a therapeutic measure. In 1932, Ochsner (2), who treated a series of cases suffering from chronic bronchiectasis by the intratracheal use of iodized oil, reported results superior to other methods of treatment. In 1933, Cole (3) studied the intratracheal use of the oil in a series of pulmonary cases and was pleased with the results he obtained in patients suffering from bronchial asthma. The work of these three men first stimulated our interest in the subject. Last summer, one of us (R. M. B.) had the pleasure of observing the work of Forestier in his clinic at Aix-les-Bains, France. He has used the oil in the chest primarily for the purpose of a contrast

medium: it has never been used by the French as a therapeutic measure in asthma (4).

During the last fourteen months, we have treated 184 asthmatic patients of various types by using iodized oil intratracheally or transnasally in connection with specific allergic management. Many of these patients were cases which we had had under our care for from two to four years. In the patients suffering from periodic attacks of asthma with periods of absolute freedom, the combined treatment gave definitely better results than allergic management only. The results of the combined treatment in the intractable type, as compared with the usual method of treatment, were in many cases very striking and have encouraged us to make a report on the use of iodized oil in conjunction with specific desensitization in 50 cases of intractable asthma, most of which we have had under our care for from six months to four years.

Dual Etiology of Intractable Asthma.—Why many asthmatic patients have periodic attacks of asthma throughout life but are entirely free from symptoms between attacks, while others, either early in life or during middle or old age, suffer continuously from mild to severe attacks or at least cough and raise purulent mucus between attacks, is a question that has never been satisfactorily answered. As a possible explanation, let us consider the following history that is so commonly given by the chronic asthmatic patient:

In childhood a patient suffered from hives and eczema and had frequent bronchial colds with which he would occasionally wheeze. During the teens he was moderately free from his skin and bronchial trouble. In the twenties he developed

¹ From the Balyeat Hay Fever and Asthma Clinic, and the Department of Pharmacology, University of Oklahoma Medical School, Oklahoma City, Oklahoma.

midsummer and fall hay fever but no asthma. After ten or fifteen years of seasonal hay fever, an acute cold was encoun-

appeared for a couple of decades. Later, however, he became sensitive to midsummer and fall pollens which produced hay

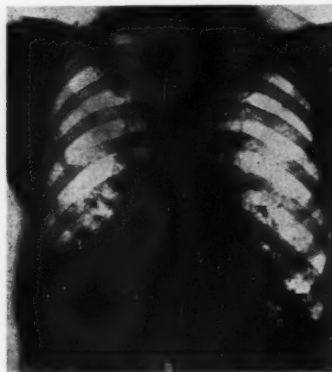


Fig. 1. Usual form of bronchiectasis. Note the large, irregular, tubular areas, and their location and connection with moderate sized bronchi. Postural drainage in this case is of value.

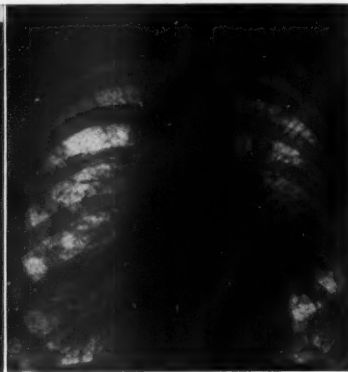


Fig. 2. Usual form of bronchiectasis. Note the sacculo-tubular area connected with a fair sized bronchus. Postural drainage was of value.

tered at the end of the season and the patient suffered with asthma for a few days. The next fall, asthma developed and persisted for two or three weeks. The fall following this, the siege lasted for six weeks. From that time on during the following year, with each cold, asthma occurred. A year or two later the attacks became much closer together, and he found that daily he either suffered from an attack of asthma or raised considerable sputum which was usually semi-purulent in type.

A study of the asthmatic over a period of years has led us to believe that what actually happened in such a case is as follows: in early life the patient became sensitive to food and to the animal epithelial group. The foods to which he was sensitive caused his eczema and hives. The food sensitization plus a sensitization to inhalants were the exciting factors in his bronchial colds. As he grew older, he automatically became desensitized to many of the foods and, therefore, lost his dermatologic symptoms. In the late teens and early twenties he naturally came in contact with less house dust, and, therefore, his asthmatic symptoms dis-

appeared for a couple of decades. Later, however, he became sensitive to midsummer and fall pollens which produced hay fever but not asthma. In middle life, after hay fever had existed for years, the repeated bronchial infections from which he suffered each fall produced not only plugging of the bronchioles, but finally asthmatic bronchiectatic areas; therefore, asthma occurred at any time during the year. In the so-called intractable cases of asthma, a history somewhat similar to the one just given is usually obtained.

It appears, therefore, that patients suffering from intractable asthma may have asthma from one of two of the following sources or from a combination of both: first, the attack may be caused by edema of the bronchial tubes, due to contact with or ingestion of the substances to which they are specifically sensitive (the congestion is similar to the edema of the nasal mucosa of a hay fever patient); second, the asthmatic symptoms may be caused by mechanical plugging of the bronchioles and filling of the bronchiectatic areas, or the attack may be due to a combination of the two.

In cases of the intractable type, some patients develop attacks of asthma each night between one and two o'clock, others be-

tween three and four, and others between five and six. A satisfactory explanation of why some patients have their symptoms

Diagnostic Points Differentiating Asthmatic Bronchiectasis from the Usual Form of Bronchiectasis.—In the study of the chronic

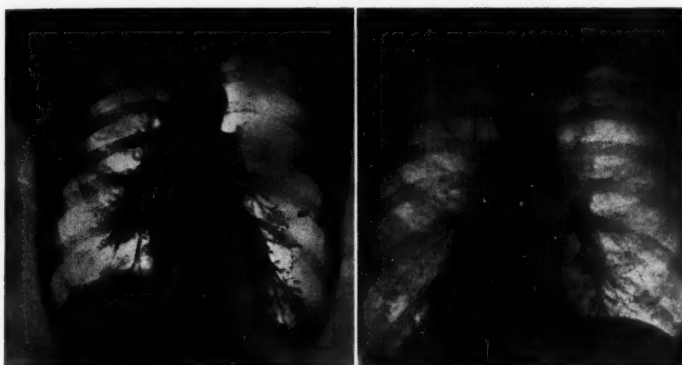


Fig. 3 (left). Asthmatic bronchiectasis (saccular form). Note the multiple pus pockets, their size, location, and their connection with small bronchioles. Postural drainage in this case was not productive, but brought on severe attacks of asthma.

Fig. 4 (right). Asthmatic bronchiectasis (tubular form). Note location and the fact that many of the bronchial branches are larger than the stem.

early in the night and others later has never been given. When one considers the mechanics of the bronchial tubes, the following explanation seems plausible. In one individual the amount of mucus produced is fairly great, and, therefore, it requires only from two to three hours after retiring for enough mucopurulent material to collect in the bronchioles or in the bronchiectatic sacs to demand a "cleaning-out process," which is an asthmatic attack. In another individual it takes from four to five hours, and in another, six to seven hours for a sufficient amount of mucopurulent material to collect to require the mechanical procedure to take place. For this reason, in one case the attacks should occur each night about two o'clock, in another at three to four o'clock, and in the third at five or six o'clock in the morning.

In determining etiologic factors and planning therapeutic measures in intractable asthma, we believe that careful consideration should be given not only to the specific sensitization findings, but also to the local pathology of the bronchial tree produced by repeated superimposed infections on the hypersensitive bronchial mucosa.

asthmatic, we have found many who raise enormous quantities of purulent sputum, which usually does not occur at one time but is distributed throughout the day. The sputum ordinarily does not have an offensive odor. Iodized oil bronchograms in the usual type of bronchiectasis will show the bronchiectatic area or areas connected with a fair sized bronchus or bronchi, while in asthmatic bronchiectasis the bronchiectatic sacs are usually small and located at the end of bronchioles. They are usually multiple and are often located in one section of the bronchial tree, but they may be scattered throughout a large area. Many cases show a combination of the saccular and tubular forms.

Is Postural Drainage of Value in Asthmatic Bronchiectasis?—Since the sacs of the usual form of bronchiectasis are connected with a fair sized bronchus or bronchi, postural drainage should be and is of value in relieving the patient of purulent sputum. On the other hand, since in asthmatic bronchiectasis of the saccular type the pockets are usually connected with small bronchioles, or the dilated branches in the case of the tubular type are larger than the stem,

it would be almost impossible for the thick purulent mucus to drain through the small tubes when postural drainage is attempted.

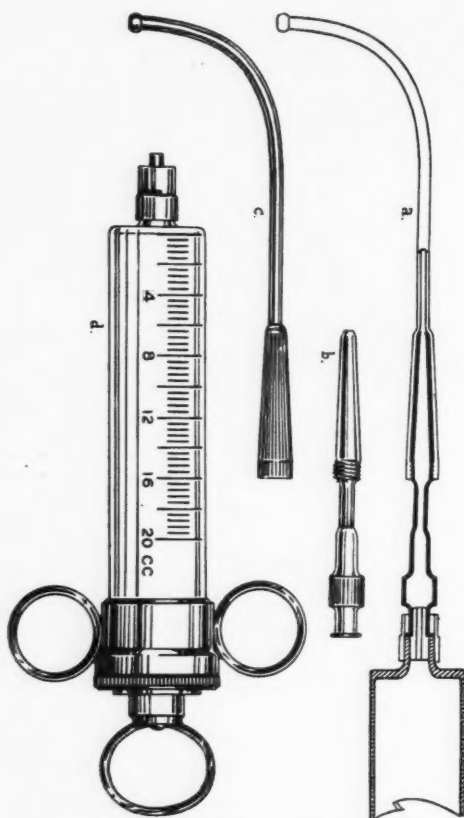


Fig. 5. Convenient syringe and laryngeal cannula for giving iodized oil.

We mention the difference in the mechanics of the two types of bronchiectasis because so many of our patients with bronchial asthma of the chronic type have often been advised to try postural drainage. Invariably the results are non-productive of sputum, but the procedure brings on a severe attack of coughing or asthma. We believe that in asthmatic bronchiectasis of either the tubular or the saccular type, postural drainage is not only not indicated but contra-indicated.

Iodized Oil Preparations Used in Diagnosis and Treatment.—In the first half of our study, we used two iodized oil preparations,

namely, lipiodol, which is said to contain 40 per cent of iodine and no chlorine, the specific gravity of which is 1.37–1.45, and lipoiodine, which is said to be ethyl-diiodo-brassidate dissolved in sesame oil, the specific gravity of which is 1.097. We found both of these oils satisfactory in the treatment of many cases, but the heavier oil was much more satisfactory for bronchograms and also for therapeutic purposes in cases of asthmatic bronchiectasis. The lighter oil was more easily given and more easily taken by the patient. Apparently it was more easily tolerated by an asthmatic patient of any type during an acute infectious process. We found the lighter oil very satisfactory in the asthmatic without bronchiectasis but whose continuous asthma was due to plugged bronchioles. The details of the two oils have been discussed in a previous paper (5).

During the last eight months, we have used almost exclusively the lighter oil, namely, lipoiodine, and one we have prepared in our own laboratory, by incorporating iodine in poppy-seed oil by the iodine chloride method. The iodine content of this oil is approximately 27 per cent, and the chlorine content 8 per cent. The specific gravity varies from 1.226 to 1.30. An ideal iodized oil to be used for bronchograms and also for therapeutic purposes in asthma should be one with moderate viscosity so as to be easily given, with fairly high specific gravity so it will not be easily coughed up, and with an iodine content sufficiently high so it will serve as a good contrast medium for delineating the bronchial tree, and, chemically, it should be a fairly stable oil. These properties we have found in the oil which we are using that contains iodine and chlorine.

Technic of Giving Iodized Oil.—There are three methods of injecting iodized oil into the bronchial tubes, namely, transtracheal, transnasal, and intratracheal. The first and third methods were described originally in detail by Sicard and Forestier (6), and more recently Forestier (4) has described the second method. Due to the fact that the transtracheal method is quite



Fig. 6. Position of patient for filling lower section of right bronchial tree.



Fig. 7. Position of patient for filling lower portion of the left bronchial tree.

complicated, it is not practical as a routine procedure for giving iodized oil for bronchographic purposes or as a therapeutic measure: under unusual conditions it might be indicated. The transnasal method, one used rather extensively by Forestier at the present time, we have found to be fairly satisfactory in patients who seem to take the oil with difficulty by the intratracheal method; however, these patients are rare. The latter of the three methods, namely, the intratracheal, is the one of choice as a routine procedure.

The exact method of giving the oil intratracheally varies greatly in the hands of different operators. The method we are now using is a combination of Cole's (3), Singer's (7), and Ochsner's (2). It has previously been described by us (5). However, during the last six months we have considerably modified the method which we previously described. In brief, our present method of giving oil intratracheally is as follows:

Preparation of the Patient.—The bronchial tree of the intractable case of asthma usually is accustomed to considerable irritation; therefore, the introduction of a small amount of a non-irritating oil usually is not disturbing to the patient. When the oil is to be given, either for the purpose of a bronchogram or as a therapeutic measure, if the patient is wheezing or coughing he

should have from 6 to 10 minims of adrenalin a few minutes prior to its introduction. The adrenalin decreases the amount of edema of the bronchial tubes and also allows the patient to bring up a considerable amount of mucus, thereby permitting the oil to better penetrate the bronchioles and the bronchiectatic areas. If the asthmatic also suffers from the usual form of bronchiectasis, postural drainage should first be given.

The patient is advised to come for his oil without breakfast, just before the noon lunch, or prior to the evening meal, as the gag reflex and tendency to nausea are less at these periods.

Just prior to giving the oil the first time, especially if a bronchogram is to be made, which always should be done in the chronic asthmatic, the throat of the patient should be sprayed with a 2 to 4 per cent solution of cocaine hydrochloride while he breathes deeply, so as to allow the spray to reach the bifurcation of the trachea. The cocaine reaching this area will help to overcome the cough reflex. After taking the oil for the first time, the patient realizes there is no pain connected with the procedure, very little discomfort, and that the cocaine is bitter, and from that time on the oil usually can be given without local anesthesia and without any difficulty.

Preparation of the Oil.—We have learned

that if the oil is warmed to about 110° F. it is very satisfactory, both for bronchographic and therapeutic purposes. At this

and he should remain in that position from five to ten minutes. The more nearly horizontal position is required on the left side be-



Fig. 8. Note the angle the left bronchus makes with the trachea.

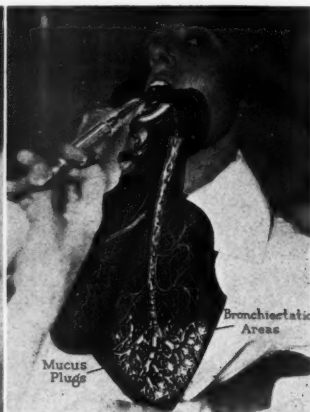


Fig. 9. Diagrammatic sketch. Note position of the point of the laryngeal cannula.

temperature the viscosity is such that the oil penetrates the plugged bronchioles well and enters the bronchiectatic areas, if they be present, and yet sufficient quantity will stick to the walls of the bronchial tubes to delineate them well.

Instrument for Giving Iodized Oil.—An instrument for giving the oil is shown in Figure 5. A 20 c.c. Luer-Lok Control syringe is used. This is ideal providing one is treating a large number of patients; if only a few patients are cared for, a 10 c.c. B-D Luer-Lok Control syringe is just as satisfactory. The laryngeal cannula we use is divided into two parts. With part *b* (Fig. 5) attached, the warm oil is drawn through into the syringe. The soft-metal laryngeal cannula tip *c* is attached as shown in *a*. The cannula as shown in Figure 5 we have found to be very convenient, but the regular B-D soft-metal laryngeal cannula is quite satisfactory.

Position of Patient.—To fill the right side, the patient should be comfortably seated at a table so that he can lean to the right (Fig. 6). In filling the left side, to obtain the best results the patient should recline on the left elbow on a lounge (Fig. 7),

cause the left bronchus is often at almost a right-angle with the trachea (Fig. 8). In filling either side, the patient's head should be maintained as nearly vertical as comfort will permit. The tongue, protected by a gauze or paper napkin, is grasped and pulled well forward in order to aid in preventing the patient from swallowing.

If the patient uses very rapid, shallow breathing, the lungs will be comfortably aerated and the epiglottis will remain open. Deep breathing is not advisable, as it would start coughing.

The tip of the cannula (Fig. 9) is first placed just back of the tongue in the center line and then pulled forward so it just barely touches the root of the tongue. The barrel of the cannula should rest on the operator's thumb which is holding the tongue, a procedure which serves two purposes, namely: (1) It gives stability to the instrument; (2) if the nurse has heated the oil too high, it will be easily detected by the operator as the oil flows through the metallic cannula. The oil is given by rapid drops or in a constant stream and allowed to flow down the back of the tongue into the trachea. If allowed to drop into the

trachea instead of flowing down the wall, it produces more irritation and frequently starts coughing.

a week for two to four weeks and then changed to a seven- or ten-day interval and continued for months. As a therapeutic

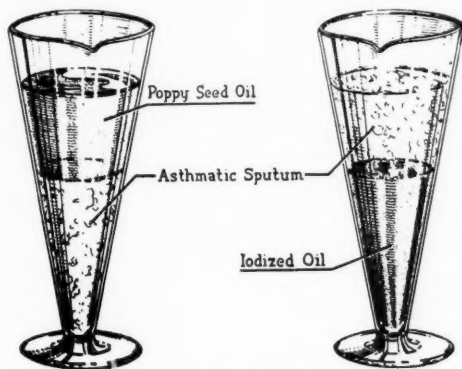


Fig. 10. Experiment *in vitro*, demonstrating what would happen if plain poppy-seed oil were used in the bronchial tubes; also, what actually happens when iodized oil is used.

Amount of Oil Used for Bronchograms and Therapeutic Purposes.—For the purpose of a bronchogram, from 15 to 20 c.c. should be given on both sides; for treatment purposes, from 5 to 10 c.c. After the oil is given, the patient should remain quiet, without coughing if possible, for five or ten minutes before the bronchogram is made. Likewise, for therapeutic purposes the patient should withhold coughing for a few minutes so as to allow the oil to penetrate the mucus-plugged tubes. Plugged bronchioles and bronchiectatic areas are practically always found in the lower portion of the bronchial tree; therefore, it is only this area that needs to be injected.

If the bronchogram shows no saccular bronchiectatic areas but only plugging or moderate dilatation of the bronchioles, the oil is given twice a week for a period of two or three weeks, using from 7 to 10 c.c. on each side at the same sitting. It is then given once a week for two to four weeks, depending on the amount of relief the patient obtains. From that time on, the oil is given at an interval of three to five weeks. If there is evidence of moderate to marked asthmatic bronchiectasis, especially if it be of the saccular type, the oil is started twice

measure, in cases with evidence of bronchiectatic areas, we have found the heavier oil much superior to the lighter.

Results of Treatment.—Of the 50 cases, all of the so-called intractable type, in which we have given iodized oil intratracheally for therapeutic purposes, 36 had been under allergic management from six months to four years, with unsatisfactory results. In all of the 36 cases, the routine treatment was not changed except that the intratracheal use of iodized oil was added, using the interval we have described. The other 14 cases, which had been under our care less than six months or were new, were all allergic, complicated with asthmatic bronchiectasis of either the tubular or saccular type. They were treated also by combining allergic management with the use of the oil, as oil in itself could not cure a patient suffering from allergic asthma.

In some of our cases, the oil has been given over a period of fourteen months. To one patient, oil has been given 45 times: the total number of times it was given to the 50 cases was 701. We observed that usually after four to six doses had been given, patients were definitely better, and occasionally improvement occurred after

the first or second dose. We have learned that in those patients whose bronchograms showed evidence of plugging of the bronchial tubes only, practical relief from symptoms was obtained after the oil had been given only a few times. Good results were not accomplished so quickly in patients whose bronchograms revealed evidence of asthmatic bronchiectasis, and usually the greater the amount of bronchiectasis, the slower was the progress. In nearly all patients in whom poor results were obtained, bronchograms revealed evidence of marked bronchiectasis.

We have classified the results of 50 cases of intractable asthma, treated by combining the use of iodized oil intratracheally with allergic management, as follows:

Very good.....	7, or 14 per cent
Good.....	28, or 56 per cent
Fair.....	6, or 12 per cent
Some relief (25 per cent).....	4, or 8 per cent
Poor.....	5, or 10 per cent

To one who has dealt with chronic cases of asthma for fourteen years and therefore knows, in the main, how unsatisfactory treatment of cases of intractable asthma based solely on allergic findings has been, the therapeutic effect of the oil is a welcome measure, but more so has it been welcomed by the chronic sufferer.

Certainly the oil is in no way curative, but only a mechanical means of freeing the pendent bronchial tubes from the plugged mucus and the bronchiectatic areas from purulent sputum, thereby not only giving the patient freedom from asthmatic spasms, but relieving him from the absorption of toxins. In many cases, we have observed patients who were temperature-free but who ran white blood cell counts from 14,000 to 18,000, which would become nearly normal or normal after the oil had been given a number of times. These patients would regain their lost appetite; their haggard appearance, doughy skin, and relaxed muscles would soon change to that of the average normal.

Contra-indications.—Ochsner (2), Cole (3), and Amberson (8) have suggested certain contra-indications, and, without ques-

tion, there are contra-indications, as we have pointed out in a previous study (5). However, it would be very unusual to find a case of chronic asthma of the type we are reporting in which the use of a non-irritating, non-absorbable oil such as iodized oil would be contra-indicated. A patient whose bronchial tubes have been infected for years and who has continually raised mucus or purulent material should theoretically tolerate such an oil with ease. However, it must always be remembered that a patient who has an idiosyncrasy to iodides will not tolerate the oil, because a small amount is broken down in the bronchial tubes, the iodine absorbed through the bronchial wall as iodides, and the remainder finally is brought up into the mouth little by little, swallowed, saponified in the jejunum, absorbed into the lacteals, lipodieresis occurs, and the iodine is liberated by the lungs and kidneys as iodides. Most of these patients, however, have taken iodides from time to time, and, therefore, a history will determine their ability to handle the oil. There are other contra-indications, as we have previously mentioned, but it would be unusual to find them in a chronic asthmatic.

Physico-chemical Mechanism.—After observing the therapeutic value of iodized oil as an agent for temporary relief in patients suffering from asthma of the intractable type, we became very much interested in its physico-chemical mechanism. The fact that we (5) could find iodine in the urine of a patient from thirty to forty minutes after the oil had been given intratracheally, and in large amounts from two to five hours later, made us feel, as did Forestier (4), that in the bronchial tubes, in some way, a fat-splitting process had taken place. It occurred to us that the iodides passed through the bronchial wall, and, by so doing, changed the polarity of the goblet cell of the bronchial mucosa, thereby checking the formation of the white glairy mucus. Experimental work, which we did by injecting the oil into the bronchial tubes of dogs, led us to believe that if a fat-splitting process took place in the bronchial tubes,

it was not an early procedure, because after four hours no iodine could be found in the urine of the dogs.

Our experimental work with dogs naturally leads us to believe that, when iodized oil is injected into the bronchial tree of the



Fig. 11. Bronchogram of a patient to whom iodized oil had been given once. Note the many small mucus plugs.



Fig. 12. Bronchogram of a patient to whom oil had been given several times. The bronchial tubes and bronchioles are well filled.

Sicard and Forestier (6) have recorded in their book, "The Use of Lipiodol in Diagnosis and Treatment," a table showing the rapid elimination of iodine through the bronchial wall in the human. In talking with Forestier, we called his attention to our experimental work on dogs, which indicated that iodine was not absorbed through the bronchial wall during the first three or four hours, and he suggested the possibility that the iodine-freeing process took place only after several hours of contact with the bronchial mucosa.

As a means of determining what happens to iodized oil retained in the bronchial tubes from three to five days, we (10) gave repeated intratracheal injections of iodized oil (lipiodol—same as used by Forestier) to a series of dogs; to another group the oil was given through an intubation tube so no oil could be brought back into the mouth and swallowed. In brief, the results were as follows: the dog of the first group excreted, by the kidney, 236 mgs. of iodine on the second day, while the dog of the second group showed an output in the urine of 15 mgs. of iodine, having excreted the largest amount of iodine in any one twenty-four-hour periods.

asthmatic patient, a small amount breaks down in the bronchial tubes, either by the process of oxidation or by a fat-splitting enzyme, but that most of the oil is brought up into the mouth, swallowed, saponified in the jejunum, and absorbed into the lacteals before iodine is liberated.

Ochsner (2 and 9) believes that the beneficial effect of the intratracheal use of iodized oil in bronchiectasis and also in chronic asthma is partially due to its bactericidal effect. It appears to us that if there is a bactericidal effect, it would have to be due to one of the two following sources: (1) the presence of the oily substance itself, or (2) to free iodine. To determine the possible effect of the first factor, we added iodized oil to tubes of asthmatic sputa and incubated them 48 hours. The bacterial growth in these tubes was no less than the controls. It is true that Ochsner (2) found the bacterial count of the sputa from the bronchiectatic patients to whom he gave repeated intratracheal injections of iodized oil to decrease. This can be explained by the fact that the heavy oil is constantly replacing the purulent material. The new bronchial secretions formed in the large bronchial tubes naturally are

much less purulent than the material in the bronchiectatic areas. In considering the second factor, we must not forget the state-

chanical. In explaining the mechanical therapeutic effect of the oil, one must take into consideration its physical properties.

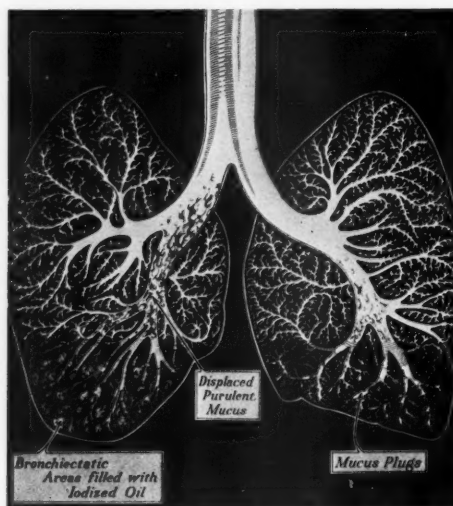


Fig. 13. Diagrammatic sketch demonstrating mechanical effect of iodized oil. Note replaced mucus.

ment of Sollmann (11): "Free iodine cannot be liberated in the body, since all conceivable reactions for the liberation of iodine from its compounds require much higher hydrogen ion concentration than exists anywhere in the body." The only exception he makes is in case of gastric juices in which the acidity may be sufficient to liberate iodine. Iodine that is apparently liberated in the bronchial tubes instantaneously becomes sodium or potassium iodide. It appears that the second factor, namely, free iodine, as a bactericidal agent must be forgotten. It is possible that the small amount of iodine that is liberated, which becomes sodium or potassium iodide, may help in liquefying the tenacious mucus in the bronchioles, just as it does when iodides are administered by mouth.

After giving the oil in our clinic 3,240 times and watching its effect on various types of asthma, including the intractable type, and after reviewing very carefully our experimental work, we believe that the therapeutic value of the oil is primarily me-

Note the specific gravity of the following products.

Asthmatic sputum.....	Sp. gr. 1.012
Plain poppy-seed oil.....	Sp. gr. 0.910
Sesame oil.....	Sp. gr. 0.916
Lipiodine.....	Sp. gr. 1.097
Iodized oil prepared in our own laboratory, 35 per cent	Sp. gr. 1.226-1.30
Lipiodol, 40 per cent.....	Sp. gr. 1.37-1.45

The 35 per cent iodized oil which we are using almost exclusively at the present time is made by iodizing the poppy-seed oil with iodine chloride. It is obvious, therefore, that the oil contains both iodine and chlorine. Prepared by this method, the oil is slightly viscous, pale amber, and is a neutral liquid with an oleaginous taste (resembling "cooked" oil) and has a specific gravity of 1.228 at 25° C. It contains no free iodine. After it stands for several weeks in the dark, there is no color change, and neither is there free acid nor free iodine. Some darkening is observed when the product is exposed for the same length of time to light, but repeated tests will not show the presence of free iodine or free chlorine.

It is important to point out that the presence of chlorine makes the oil in no way objectionable, clinically. On the other hand, we have evidence to indicate that its presence actually lends increased stability. Its gravity is sufficiently greater than asthmatic sputum to be an excellent replacement medium. It contains sufficient iodine to make it a good contrast medium.

After giving the oil the first time to a patient with plugged bronchioles, one will observe many plugs persisting (Fig. 11), while after giving it several times the bronchogram will appear (Fig. 12). During or just following the giving of the oil to one with asthmatic bronchiectatic areas, the patient will frequently cough, but instead of raising oil, purulent asthmatic sputum will be brought up. Consider what would happen to the plugged bronchial tubes and bronchiectatic areas when iodized oil is given (Fig. 13).

We feel, after careful experimental work with animals and a clinical study of the intratracheal use of iodized oil in patients with intractable asthma, that its efficacy lies (1) in the mechanical coating over of the bronchial mucosa of the pendent tubes, preventing contact with the allergenic substances; (2) by lubricating the bronchial tubes, thereby preventing plugging; (3) by replacing the purulent material in the bronchiectatic areas so as to prevent the absorption of toxins, and (4) after the oil is brought up, swallowed, saponified, absorbed, and lipoidieresis takes place, it is partially eliminated by the bronchial tubes, giving an effect similar to the use of iodides by mouth. Therefore, it appears that the therapeutic value of iodized oil given intratracheally is both chemical and mechanical, but its primary value lies in its replacing and lubricating action.

CONCLUSIONS

1. Most cases of intractable asthma have a dual etiology, namely, a specific sensitization factor and also a mechanical condition produced by tenacious mucus or purulent material, either of which can produce asthmatic attacks.

2. Asthmatic bronchiectasis, which commonly occurs in intractable asthma, clinically and mechanically differs from the usual form of bronchiectasis. Postural drainage is not indicated in asthmatic bronchiectasis.

3. In the treatment of intractable asthma, we believe that consideration should be given not only to the specific sensitization findings, but also to the mechanical condition of the bronchial tubes due to the local pathology of the bronchial tree which, in turn, is produced by repeated superimposed infections on the hypersensitive bronchial mucosa.

4. An ideal medium for the treatment of the mechanical factor in intractable asthma is an iodized oil. An ideal iodized oil should have the following properties: non-irritating, non-absorbable, moderate viscosity, a sufficient gravity (1.225-1.40) so the oil is not easily coughed up, and an iodine content sufficiently high to make it a good contrast medium for bronchographic purposes.

5. The intratracheal method of administering the oil is the one of choice, both for diagnostic and therapeutic purposes.

6. Usually, only the lower section of the bronchial tree need be injected when the oil is used as a therapeutic measure in asthma. The filling of the left lower section is somewhat difficult; the correct position of the patient is important.

7. For bronchograms, 15 to 20 c.c. of iodized oil should be put on each side. For therapeutic purposes, from 5 to 10 c.c. should be given at weekly, biweekly, or monthly intervals.

8. Of the 50 cases of intractable asthma in which poor results had been obtained by allergic management, very good or good results were obtained in 70 per cent by combining the use of iodized oil intratracheally with allergic management.

9. In the treatment of chronic asthmatics, contra-indications are not many; the intolerance to iodides is the one most commonly encountered.

10. The therapeutic value of iodized oil given intratracheally to the intractable

asthmatic appears to be due primarily to the mechanical effect of the oil.

11. The heavier iodized oils are excellent contrast media for delineation of the bronchial tree.

12. The intratracheal use of iodized oil cannot, in itself, cure a patient suffering from allergic asthma, but it is of inestimable value as a means of forcing up bronchial plugs and replacing pockets of pus with a non-irritating, non-toxic substance.

13. In the treatment of intractable asthma, eliminative measures and desensitization against the substances to which the patient is specifically sensitive, are of first importance. From our present study, we are led to believe that the intratracheal use of iodized oil in the bronchial tubes is next in importance. A combination of the specific and the mechanical is ideal treatment in cases of intractable asthma.

14. After using iodized oil in the treatment of asthma of various types over a period of fourteen months, we feel that it is an indispensable measure in the treatment of cases of intractable asthma.

REFERENCES

- (1) ANDERSON, WILLIAM: Some Observations on the Value of Intratracheal Injections of Iodized Oil for Bronchial Asthma. *Jour. Allergy*, November, 1932, 4, 44.
- (2) OCHSNER, ALTON: Diagnosis and Treatment of Bronchiectasis. *South. Med. Jour.*, February, 1932, 25, 149.
- (3) COLE, DEAN B., and HARPER, EDGAR C.: Therapeutic Use of Iodized Oil in Pulmonary Disease. *Jour. Lab. and Clin. Med.*, April, 1933, 18, 704.
- (4) FORESTIER, J.: Lecture before medical students, University of Oklahoma Medical School, Oklahoma City, November, 1934. Personal communication.
- (5) BALYEAT, RAY M., and SEYLER, EVERETT L.: The Therapeutic Value of the Intratracheal Use of Iodized Oil in Bronchial Asthma. *Journal-Lancet*, September, 1934, 54, 18.
- (6) SICARD, J. A., and FORESTIER, J.: The Use of Lipiodol in Diagnosis and Treatment. Oxford University Press, 1932.
- (7) BALLON, H., SINGER, J. J., and GRAHAM, E. A.: Bronchiectasis. *Jour. Thoracic Surg.*, December, 1931, 1, 154; February, 1932, 1, 296; April, 1932, 1, 397; June, 1932, 1, 502. Also, personal communication.
- (8) AMBERSON, J. BURNS, JR., and RIGGINS, H. McLEOD: Lipiodol in Bronchography: its Disadvantages, Dangers and Uses. *Am. Jour. Roentgenol. and Rad. Ther.*, December, 1933, 30, 727.
- (9) OCHSNER, ALTON: Personal communication.
- (10) SHOEMAKER, H. A., and BALYEAT, RAY M.: Unpublished paper, December, 1934.
- (11) SOLLMANN, T.: *Jour. Pharmacol.*, 1916-17, 9, 269.

SIMULTANEOUS MULTIPLE FIELD IRRADIATION WITH A 4.5-GRAM RADIUM PACK¹

By M. C. REINHARD and H. L. GOLTZ, *Buffalo, N. Y.*

From the State Institute for the Study of Malignant Disease, Buffalo, N. Y.;
Burton T. Simpson, M.D., Director

IN 1930 a radium pack was designed and constructed as described in two previous papers (1, 2) to contain four grams of radium. The radium was distributed in 100-milligram tubes over an area 8×8 cm., each radium tube

treating large lesions located at or near the surface. When treating deep-seated lesions, however, such as those of the mid-pelvic region, this wide spreading of the beam prevents a close spacing of adjacent fields, particularly when multiple ports of

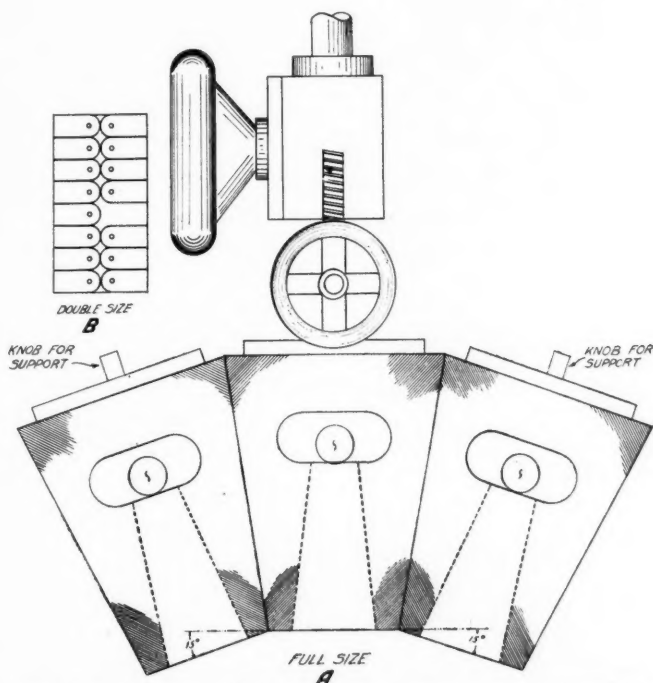


Fig. 1-A. Assembly drawing of the three-section pack showing relation of various parts.

Fig. 1-B. Arrangement of the 100 mg. tubes in the tray.

radiating the entire field of 10×10 cm., at either 6, 10, or 15 cm. radium-skin distance. The large radiating area and field size results in extreme spreading of the beam after it leaves the pack, especially at the shorter distances. This characteristic is a decided advantage when

entry are used to produce a cross-firing effect at depth. It was found that with this pack at a radium-skin distance of 10 centimeters, two anterior and two posterior ports could be used to advantage, provided a distance of 5 centimeters was maintained between the ports on each skin surface, and that the angle did not exceed 15° .

¹ Received for publication Jan. 10, 1935.

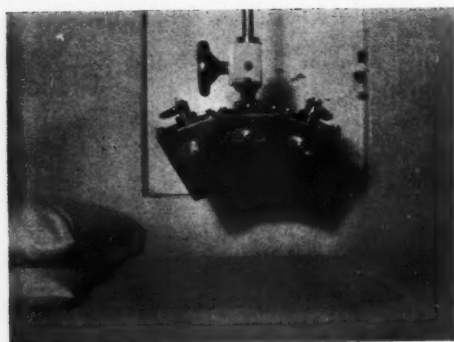


Fig. 2. View of the three-section pack showing angulation (15°) of the individual sections. This angle may be increased by inserting wedges between the sections.

This arrangement produced a depth intensity of 63 per cent at the midpoint of a pelvis 20 centimeters antero-posterior dimension. Because of the field size and the space required between adjacent fields, it was impossible to apply more than two fields with this pack to either the anterior or the posterior surfaces of such a pelvis. Two lateral fields could, of course, be used in addition to the two anterior and posterior fields, but the distance from these

lateral fields to the interior was too great to cause a sufficient increase to warrant their use; moreover, the skin areas on those surfaces adjacent to the treatment area would receive considerable radiation from the lateral port, due again to the extreme flare of the beam. Actual estimation by means of isodose charts, of the intensity at depth with two anterior, two posterior, and two lateral ports, showed that the intensity at the 10 cm. depth had increased to only 66 per cent, with all skin areas receiving 100 per cent at a radium-skin distance of 10 centimeters. Greater intensities than these were desired, in order to effectively radiate the deep-seated lesions. Of course, a greater intensity could be obtained for mid-pelvic regions, by using the pack at a distance of 15 centimeters, but the treatment time would be lengthened to such an extent, especially with multiple ports, that this method was found to be impractical with the amount of radium available. Furthermore, at this distance, more radiation penetrates to the opposite skin surface, which necessarily reduces the dose which can be applied to

CHART I

	New Pack		Four-gram Pack		
	1 Section	3 Sections			
Ra.-S. D.	10 cm.	10 cm.	6 cm.	10 cm.	15 cm.
Surface Int.	63 r/gm.-hr.	69 r/gm.-hr.	86 r/gm.-hr.	50 r/gm.-hr.	28.5 r/gm.-hr.
Depth	%	%	%	%	%
0 cm.	100.0	100.0	100.0	100.0	100.0
1	88.8	91.0	87.5	91.0	91.0
2	76.5	80.0	71.5	76.0	80.5
3	65.3	72.5	59.1	65.1	71.0
4	55.0	67.6	49.3	56.1	62.0
5	46.6	64.0	41.3	49.0	54.0
6	40.0	60.8	34.7	42.4	47.5
7	33.3	58.0	29.1	36.7	42.0
8	29.5	55.0	24.6	31.8	36.7
9	25.6	51.6	21.3	27.5	32.3
10	22.2	48.0	18.7	24.0	28.5
11	19.9	43.8	16.6	21.3	25.7
12	16.7	39.3	14.9	19.0	23.5
13	13.3	35.0	13.3	17.3	21.2
14	12.2	31.2	12.0	15.6	19.3
15	10.5	27.8	10.8	14.2	17.5
16	8.6	25.0	9.8	13.0	16.2
17	7.1	22.2	8.9	11.8	14.8
18	5.9	20.1	8.0	10.8	13.5
19	4.8	18.5	7.3	10.0	12.3
20	3.8	17.0	6.7	9.1	11.5

The surface intensities as listed include tissue scattering.

that skin surface and, therefore, reduces the dose in the mid-pelvic region.

In order to produce a greater intensity

are parallel to one another and there is a space of 3 centimeters between adjacent fields. Each section is inclined 15 degrees

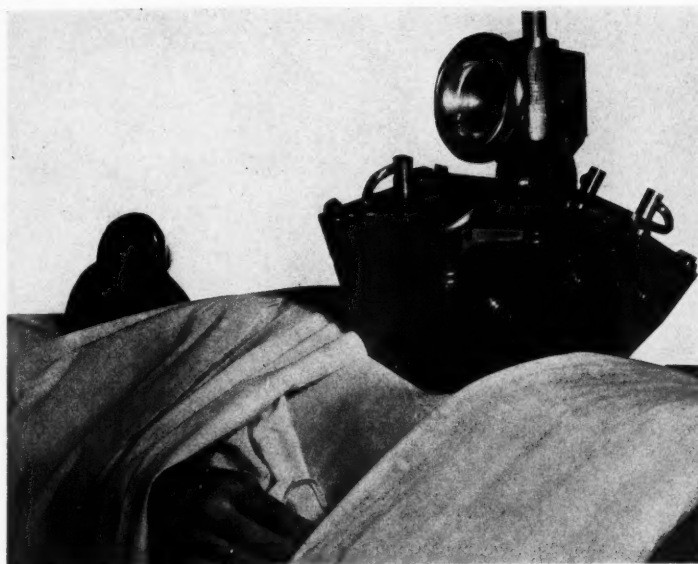


Fig. 3. Three-section pack applied to a patient.

at depth by the utilization of more ports of entry, it was decided to remove the radium from the 4-gram pack, and redistribute it in a pack of radically different design and purpose.

This new pack (Figs. 1, 2, and 3) is essentially a three-cannon arrangement, or three separate packs arranged in a manner not unlike that of Mallett and Danne. Each cannon, or section, is a unit in itself, and may be used singly or in any combination. The radium is contained in three removable trays, in each of which there is 1.5 grams of radium, making a total of 4.5 grams in the pack as a whole. The radium tubes were arranged in each tray to occupy as small a space as possible (Fig. 1-B). The radiation from each tube was spread over a rectangular area 5.4×9.3 centimeters. This arrangement in each cannon, unlike the 4-gram pack, reduces the extreme flare of the beam (Fig. 4) and permits a closer spacing of the fields. The long axes of the three fields

from the neighboring section. For most work, when the three sections are used as a unit, the long axes would be applied parallel to the long axis of the body. The radium-skin distance of this pack is 10 centimeters. At this distance with the smaller field size, the careful arrangement of the individual radium tubes observed in constructing the 4-gram pack, is not essential.

In a previous paper (3) it was pointed out that when the radium tubes are in a perpendicular position as they were in the former 4-gram pack, the intensity may be reduced as much as 20 per cent, due to the fact that the lower layers of radium act as a filter and remove some of the gamma rays. In the new pack, this so-called "intrinsic filtration" was avoided to a large extent by placing the tubes in a horizontal position. Subsequent measurements showed a gain of 26 per cent, over the former 4-gram pack, due in part to the close arrangement of the radium tubes

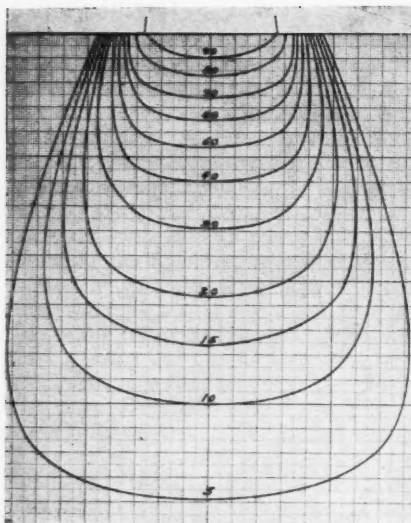


Fig. 4. Isodose chart for single section when used separately.

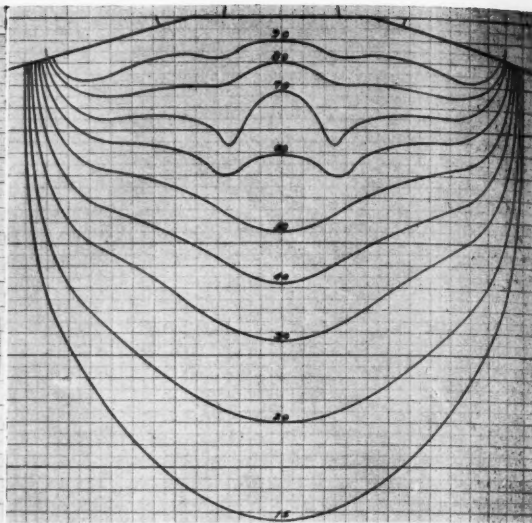


Fig. 5. Isodose chart for the three-section pack.

and in part to the difference in the height of the radium column.

The fact that the trays containing the radium are removable makes this arrangement as flexible as possible. For example, two of the trays may be inserted into the former pack, so that it may be used on those particular lesions for which it is best suited, or the cannons may be separated and each may be suspended as an individual pack, making it possible to treat three patients at one time.

The beams emitted from a single section and from the three sections as a unit, were explored by a thimble ionization chamber in order to obtain values to be used in the construction of isodose charts. Figure 4 shows the isodose curve for a single cannon and Figure 5 that of the three-section pack.

The primary filter is one millimeter of platinum. The secondary filter, next the skin, consists of one millimeter of copper and one millimeter of aluminum. With this arrangement of the radium in the three cannons, as described, and the filters mentioned, the rate of dosage is 1.72 r^2

² The instrument used was a Victoreen Condenser meter calibrated in roentgens for x-ray.

per minute on the skin directly under the middle portal.

For purposes of comparison, Chart I is included, which shows the surface and depth intensities, on the central ray for the 4-gram pack, for the single cannon and the three cannons as a unit. It can be seen readily from this chart that the depth intensities have been greatly increased by this arrangement.

Application of this pack to the anterior and posterior surfaces of a patient 20 centimeters in antero-posterior dimension, produces an intensity at a depth of 10 centimeters or at the midpoint of the pelvis, of 82 per cent, with all the skin surfaces receiving 100 per cent. This depth intensity is the same as that produced by x-rays of effective wave length 0.16 \AA . at 80 centimeters T.S.D. with a field size of 20×20 centimeters.

The volume of tissue irradiated with this method is considerably less than when four fields are radiated by the 4-gram pack, or even when two fields are radiated with x-ray with the 20×20 centimeter field at 80 centimeters distance. Whether this decrease in the total volume irradiated with the accompanying decrease in the

amount of healthy tissue damage, together with the increased depth intensity will prove to be an improvement over previous methods, remains to be determined. Some research on the treatment of deep-seated lesions with this pack is now in progress.

SUMMARY

A cross-firing 4.5-gram radium pack is described. Charts showing surface and

depth intensities as well as isodose curves are presented.

BIBLIOGRAPHY

- (1) REINHARD, M. C.: A Four-gram Pack. *Am. Jour. Cancer*, 1933, **17**, 763.
- (2) SCHREINER, B. F., WEHR, W. H., and REINHARD, M. C.: The Four-gram Radium Element Pack: Some Possibilities by External Radiation. *Arch. Phys. Ther., X-ray, and Radium*, 1933, **14**, 293.
- (3) REINHARD, M. C., and GOLTZ, H. L.: Intensities from Various Radium Packs. *Am. Jour. Cancer*, 1934, **22**, 359.

HYPERINSULINISM: THREE CASES RELIEVED BY RADIATION¹

By S. C. BARROW, M.D., *Shreveport, La.*

THE disease entity hyperinsulinism, accompanied and characterized by certain symptoms, the result of hypoglycemia, was first brought to the attention of the profession by Harris (1), in 1924. Shortly after the discovery of insulin by Banting in 1922, reports of cases receiving overdoses began to appear. The symptomatology noted in these cases resembled so closely symptom-complexes frequently observed in certain patients in whom pancreatic disease had not been suspected and in whom insulin had not been given, that a relationship as to cause was the logical conclusion in Harris' mind.

In his first communication, he reported two cases—non-diabetic patients who had not received insulin—in which the symptoms observed were identical with certain other cases which were known to have received an over-dose of insulin. Both of these cases had low blood sugar, and in each the symptoms were controlled by carbohydrate diet.

If a certain group of cases, receiving an over-dose of insulin, showed the same symptom-complex as another group that had not received insulin, Harris reasoned that there must be existing in this latter group, spontaneously, an excess of insulin. Hence the term hyperinsulinism, an over-secretion of the islets of Langerhans which Harris considers a disease analogous to hyperthyroidism, hyperpituitarism, hyperadrenalism, etc. Incidentally he argues that "hypoinsulinism" would be a preferable term to describe diabetes or hyperglycemia.

The symptoms of hyperinsulinism, while protean, are generally familiar to the profession to-day; the procedures in arriving at a diagnosis and the methods of treatment are somewhat standardized, but the etiology in many cases remains unsettled

and unexplained. Hyperinsulinism is a disease of the pancreas, although hypoglycemia, its distinctive and constantly accompanying condition, may be due to disease of other organs or secreting glands.

The first case of unconsciousness and convulsions, proven to be due to hyperinsulinism, was reported by Allen (2) in 1928. Autopsy in this case showed carcinoma of the pancreas with metastasis to the liver, the metastatic areas in the liver showing islet cells with insulin production. Allen (3), in 1928, reported two other cases of hyperinsulinism with recurring attacks of convulsions. In 1929, Howland (4) reported the first case of hyperinsulinism, showing convulsions and coma, which was cured by surgical removal of an adenoma of the pancreas. In 1931, Car (5) reported a case, a boy 18 years of age, diagnosed as adenoma of the pancreas, who was cured by operative removal of the adenoma. This patient was having convulsions and marked hypoglycemia. In 1932, Womack, Grogg, and Graham (6) reported the removal from the pancreas of a small adenoma, with cure of hypoglycemia and relief of mental confusions and unconsciousness.

These cases, along with many others of a similar nature that have now accumulated in the literature, seem to prove that adenomas of the pancreas are definite etiologic factors in producing hyperinsulinism with resulting hypoglycemia.

Operative and autopsy findings in other cases have disclosed simple hyperplasia of the islet cells, hypertrophy, and, at times, no microscopic changes in the pancreas whatever.

Harris, Taylor, Graham, and Chilton (7 and 21), in 1932, reported a case of hypoglycemia that had had recurring attacks of unconsciousness, in which their successful removal of one-half of the pancreas, which showed no adenomas, resulted in a cure. This is the only case without adenomas re-

¹ Presented before the Radiological Society of North America, at the Twentieth Annual Meeting, in Memphis, Tenn., Dec. 3-7, 1934.

ported in which resection of part of the pancreas gave a clinical cure. In a personal communication to Dr. Harris (22) and quoted by him, Graham mentions a case of a child 15 months old, upon which he operated, removing seven-eighths of the pancreas, thereby relieving all hypoglycemic symptoms. In 1928, Finney (8) removed a portion of the pancreas for hyperinsulinism; in 1930, Judd (9) did a similar operation, but in each case the results were disappointing. In all cases in which operative removal of portions of the pancreas has been done, with the exception of Harris' case, which was one of narcolepsy, poor results followed unless adenomas were present.

Cases of hyperinsulinism operated upon and autopsy findings have disclosed that the following are present in some: adenoma; carcinoma; simple hyperplasia or hypertrophy of islet cells, and a normal pancreas. Thus, intrinsic to the pancreas, we have the following as etiologic factors: adenoma; carcinoma; hyperplasia or hypertrophy, and simple functional changes to which may be added, according to Harris (10), trauma and chronic infections. Patterson and Elliott (23) have just reported several cases of hypoglycemia, cured after removal of infected gall bladders.

However, in a discussion of the etiology of hyperinsulinism, the interdependence existing between the insulogenic function of the pancreas, the adrenals, the pituitary, the thyroid, and other hormone-producing glands, must not be forgotten.

The terms hyperinsulinism and hypoglycemia are not in any sense synonymous. Hypoglycemia develops as a condition, in many organic disfunctions, independent of pancreatic disease, just as tachycardia exists in many conditions other than hyperthyroidism, though it is a constant symptom of thyroid hyperactivity. The symptomatology of hyperinsulinism, arising spontaneously, is identical with that resulting from an over-dose of insulin given therapeutically.

Tedstrom (11), in analyzing 65 reported cases, found the following symptoms

occurring: stupor and coma, in 46; weakness and fatigue, in 47; muscular twitchings and convulsions, in 34; change of general behavior, mental confusion, and restlessness, in 40; speech disturbances and eye symptoms, in 30; loss of memory, in 20; sweating, in 19; hunger, in 12; dullness, listlessness, and drowsiness, in 19; fainting, nausea, and vomiting, in 18. In 14 out of the 65 cases, a diagnosis of idiopathic epilepsy had been made; thus, those characteristic symptoms found in petit and grand mal may be added to the above list. The disease, according to Weil (12), is said to occur twice as often in males as in females and may make its appearance at any age, in colored as well as in whites. Brower (13) quotes Layton as stating that in the 500 cases he had had under observation, mental symptoms were dominant, many acting as if they were demented or intoxicated. In a study of 16 cases which he personally treated, Powell (20) reports that all showed mental symptoms, and he concludes that normal brain function is dependent on normal sugar concentration.

The symptoms may be constant in mild forms, or intermittent in mild and severe forms. In the constant and mild forms, we have the dull, stuporous, dumb individual with periods of restlessness, irritability, nausea, vomiting, vertigo, profuse sweating, hunger, mental confusion, weakness, tremors, nervousness, etc. In the severe forms these symptoms may be exaggerated, terminating in convulsive seizures and coma. In all cases, excepting in the terminal stages, the symptoms are controlled and severe attacks aborted by administration of carbohydrates.

According to Briggs (14), physical and laboratory examinations, except during an attack, may reveal no pathognomonic sign of disease. During an attack, the picture resembles either an insulin reaction or an epileptiform state. The outstanding characteristic of the attacks, however, is the fact that they are at once relieved by carbohydrate feeding. The attacks or exacerbations of symptoms usually occur at hours when there has been a long interval since

eating, early in the morning, or after a late or missed meal. Also, prolonged mental or physical exertion may precipitate an attack.

The diagnosis of hyperinsulinism rests upon the determination of a low blood sugar, though it must be remembered that low blood sugars have other causes than excessive insulin secretion.

Joslin (15) says that normal fasting blood should show 100 mg. of sugar per 100 c.c. of blood. Like other normals, a reasonable percentage above or below is still classed within the normal limits. Low blood sugars do not react the same in all individuals. A hypoglycemia of 50 mg. may develop no reaction in one, while in another, it may precipitate convulsions and coma. Low fasting sugar or low sugar, from three to six hours following a glucose meal, was noted by Tedstrom (11) in every one of 65 cases examined by him. According to Bowen and Beck (16), an attack is never seen in the absence of hypoglycemia, while Johns (17) found only 54 per cent showing hypoglycemia at the time of seizure.

Harris (18) says the dextrose tolerance test usually brings out much lower blood sugar levels than simple fasting tests, and in some instances the low levels were not seen until the fourth to sixth hour.

A positive diagnosis can be made only from repeated fasting blood sugar studies and carbohydrate tolerance tests showing hypoglycemia. Weakness, hunger, nervousness, mental lapses, irritability, sweating, trembling, etc., occurring at intervals and relieved by eating, suggest a diagnosis of hyperinsulinism. If accompanied by low fasting sugar or low sugar, with dextrose tolerance tests, the diagnosis is positive.

Low blood sugar—hypoglycemia—is found in many conditions in which true hyperinsulinism does not exist. Diseases of the liver, in which the glycogenetic function is impaired, would naturally result in a reduced quantity of sugar in the blood. This is seen in extensive carcinoma of the liver, and in some cases of cirrhosis, arsenic and phosphorus poisoning, etc. A deficient

intake of proper carbohydrate diet will sometimes result in low blood sugar levels if prolonged in practice. Over- and prolonged muscular exercise and generalized disease of the skeletal muscles, such as progressive muscular atrophy, have the same result.

It is claimed that the internal secretions of the ovaries, testes, and parathyroids are synergistic with insulin and tend to reduce the blood sugar, and that the secretions of the pituitary, thyroid, and adrenal glands tend to raise blood sugar. Low blood sugars from these varied sources usually are readily suspicioned and the symptomatology of disease of these organs and glands readily identified.

The treatment of hyperinsulinism by diet has rather generally resolved itself into a high fat and low carbohydrate feeding, the idea of Harris being that excessive carbohydrate intake stimulates the insulin system to increased activity. In many mild cases, this plan has worked apparent cures; in severe types, the attacks are not thus controlled and resort must be had to frequent carbohydrate feeding, as insulin is used in diabetes, with the hope of only controlling the disease.

Reference has already been made to surgical treatment of hyperinsulinism. The procedure has been eminently successful in those cases in which adenomas were present. In cases in which portions of the pancreas have been removed, in which no adenomas were found, surgical treatment has generally failed. In Harris' case (7), which resulted in a cure, it is probable that small adenomas were present but not detectable.

The hope has been expressed that surgeons may learn ultimately just how near they may approach total excision of the pancreas to effect a cure in islet hyperplasia and idiopathic cases. This may probably come true, yet to many it appeals as a search for the remedy in the wrong direction. It would seem that history may repeat itself, and the treatment followed by surgeons in cases of hyperthyroidism may find a parallel in their views of hyperinsulinism. The total removal or destruction of

an organ, particularly one whose functions are many and not entirely understood, because of certain lapses from the course of normal function, may attain a desired end, but the means are certainly not in line with what might be termed scientific procedure. Methods or the search for methods of a corrective nature, which would tend to suppress excess activity or to stimulate functional inactivity, would seem more logical and more desirable. To remove from life's activities all criminals, near criminals, and potential criminals, no doubt would meet the wishes without disturbing the consciences of those with radical reform ideas, but it certainly would not square with the tenets of a true civilization.

The inhibitory action of radiation on all secretory glandular tissue, especially when in a hyper-functioning state, is well known to those members of the profession who have studied its effects or observed its action: time will not permit a detailed review of the action of radiation in this respect.

Desjardins (19) gives a complete review of all experiments relative to the effects of radiation on the pancreas. Of interest to us are the experiments of Tsuzuki, 1926, which showed a distinct atrophy of the islands of Langerhans in rabbits after short wave radiation. A careful review of all the literature which we have been able to assemble shows no reference to the treatment of hyperinsulinism by radiation, except the case reported by the writer in *RADIOLOGY* of September, 1933 (page 296). This case, along with two others which are reported below, offer a suggestion for the further use of radiation as a possible agent in the treatment of hyperinsulinism of pancreatic origin.

Case 1. D. W., a white female, age 9 years, weight, 65 pounds, height, 52 inches, whose general physical appearance was healthy, although she was mentally dull, listless, and inattentive. However, after eating, her expression would change to that of a person with normal mentality. Her physical examination disclosed no defects; Wassermann was negative; feces, blood counts, and basal metabolism were normal.

Her father, mother, one brother, and two sisters all seemed healthy and normal in every way. However, one aunt, aged 21 years, had been a confirmed epileptic since the age of 17 (Case 2). Otherwise the family history was negative.

When the patient was 5 years of age, her mother noted that the child at times seemed to be dull, listless, and stuporous, while again she was bright, cheerful, and playful. After some time it was noted that her stuporous spells occurred as her meal hours neared, and disappeared after eating. As time passed, she began to have "spells" (so described by her mother) accompanied by unconsciousness. The mother gradually learned with experience to guard against these attacks by feeding. At the age of 6, the patient entered school and found it up-hill work. In the hours immediately after eating, she could learn easily, but later she would forget what she had learned, recovering it, however, as soon as food was taken.

During all this time she received no medical attention and was known by neighbors and school children as being weak-minded. About Jan. 1, 1933, Dr. Powell, of West Monroe, was consulted and, with the above history, at once suspected the true condition. Along with other laboratory tests, all of which were negative, as stated, a series of fasting blood sugar tests were made, which ran from 40 to 50 mg. per 100 c.c. of blood. On feeding every two hours, it never went higher than 73 mg. From January to April, 1933, she was kept on a low carbohydrate and high fat diet, with improvement in all symptoms.

On April 16, we administered 210 r, using 130 K.V.P., with 3 mm. Al filter, over the anterior and posterior regions of the pancreas. From April 23 to 30, her daily fasting sugar test ran from 70 mg. to 71 mg.; on May 3, the same x-ray dose was given, and from May 7 to 15, her sugar test ran from 72 to 80 mg. On May 16, June 22, and July 23, one-half the above x-ray doses was given and her blood sugar came up to 100 mg. No further x-ray treatment has been given.

Coincident with the improved blood sugar content, her general condition improved and her mentality rapidly came up to normal. She now takes zealous interest in all things that interest children of her age, and has no spells or stuporous periods.

Case 2. Miss V. W., a white female, aged 21 years, height, 63.5 inches, weight, 137 pounds, began menstruation, which was always normal, at the age of 14 years. She finished high school at the age of 18, with good grades. Being an athletic enthusiast, her general physique was above normal.

Her three brothers and three sisters were all in perfect health; her father and mother were in good health. However, she had an aunt who was subject to epilepsy, and one niece, aged 9, who suffered with hyperinsulinism. The family history was otherwise normal.

At the age of 17, she had a convulsion, during which she chewed her tongue. There were no premonitory symptoms. From then on her convulsive seizures were grand mal in type, and continued at intervals of from three or four days to thirty days. She was treated for epilepsy by several doctors, but to no avail. In May, 1933, the patient consulted Dr. Powell, of West Monroe; she was then having convulsive seizures, grand mal, from every three or four days to ten days. General physical and laboratory examinations disclosed nothing abnormal, excepting a fasting blood sugar of 45 mg., and a general mental aspect of dullness, disinterestedness, and inattentiveness, and impressed one as being stupid. She was placed on a carbohydrate diet and frequent feedings, but with no results. A change was then made to a diet of high fat and low carbohydrate content, with the result that the severity of the attacks was lessened and there was some improvement of her general mental picture.

On May 23, 1933, she was referred to us; at this time her blood sugar was running from 80 mg. to lower levels, having convulsive seizures and mental picture as described. The low carbohydrate and high fat diet

was continued and she was given radiation over the pancreas, anterior and posterior, 210 r, using 125 K.V.P., with 3 mm. Al filter. This dose was repeated one week later when her blood sugar was found to be only 60 mg.; convulsive seizures and mental picture still unchanged. On June 9, blood sugar was 66 mg., convulsions and mental picture remaining the same. On this date she was given 560 r, using 200 K.V.C.P., with 0.5 mm. Cu filter, over the pancreas, anterior and posterior. Two weeks later, June 23, her blood sugar was 90 mg.; convulsive seizures less severe and not as frequent. On this date and on July 7, the same doses were repeated, at which time the blood sugar was 100 mg. Her convulsive seizures were very light and infrequent, with a complete transformation in her mental appearance, alertness, and interest; a change to a bright, smiling, cheerful, vivacious individual, as compared to the dull, inattentive, disinterested, dumb mentality of six weeks previous. On July 21, her blood sugar was 100 mg., and during August it ran from 106 to 120 mg., during which time she had only one or two light attacks and these at times when home surroundings became such as to upset even one with a normal nerve balance.

In September, this patient developed an acute double mastoiditis, was operated upon and died.

While the results in this extreme case of hyperinsulinism were not all that were to be desired, quoting the words of Dr. Powell, under whose eye she was constantly, "It definitely indicates the inhibitory action of radiation in hyperinsulinism."

Case 3. P. T., white, male, age 5 years (normal delivery), was a thoroughly normal child for the first three years of life. Two years ago he began to have "spells," turning blue, with nervous twitchings and loss of consciousness. These spells came on at times suddenly; at other times, gradually and at times headache and pain in the stomach preceded the spells. At one time he had convulsions constantly for twenty-four hours; recently has had spells one to

two times per week, frequently early in the morning on first awakening. Attacks seem to be getting more and more severe. Between attacks, the child is bright and seemingly normal.

The patient was treated two years ago with x-rays for supposed enlargement of the thymus, with no results. He came under the care of Dr. J. D. Young, in April, 1933, at which time he was placed in the hospital where complete physical and laboratory examinations were made, which were essentially negative, except for the blood sugar, which ran, on fasting, from 72 to 80 mg. On April 24 and 25, 1933, while in the hospital, he had convulsions at 6:30 o'clock each morning: nerve sedatives and diet seemed to have little effect in relieving the condition.

On July 1, 1933, he was referred to us for treatment, at which time his blood sugar fasting was from 70 to 80 mg., all of the symptoms described above being present and seemingly increasing in severity. Between July 9 and August 21, six x-ray treatments were given over the pancreas, using 90 K.V.P., 3 mm. Al, less than a fourth erythema dose being given. On August 21, the blood sugar was 94 mg. and attacks had ceased. On Sept. 21, 1933, his blood sugar was 100 mg.; on Oct. 11, 1933, it was 106 mg. The child has had no further attacks and his mother writes that he seems to be normal in every way.

BIBLIOGRAPHY

- (1) HARRIS, SEALE: The Etiology and Prevention of Diabetes. *Virginia Med. Month.*, January, 1924.
- (2) ALLEN, F. N.: Carcinoma of Islets of Pancreas, with Hyperinsulinism. *Proc. Staff Mayo Clinic*, 2, 89.
- (3) Idem: Hyperinsulinism. *Proc. Staff Mayo Clinic*, 1928, 3, 367.
- (4) HOWLAND *et al.*: Dysinsulinism, Convulsions, Coma, Due to Islet-cell Tumor of Pancreas, with Operation and Cure. *Jour. Am. Med. Assn.*, 1929, 93, 614.
- (5) CAR, PARKER, GRAVE, FISHER, and LARIMORE: Hyperinsulinism from B. Cell Adenoma of Pancreas, Operated and Cured. *Jour. Am. Med. Assn.*, 1931, 96, 1363.
- (6) WOMACK, GROGI, and GRAHAM: Adenoma of the Islands of Langerhans: Successful Operative Removal. *Jour. Am. Med. Assn.*, 1932, 97, 12.
- (7) HARRIS, TAYLOR, GRAHAM, and CHILTON: *Jour. So. Med. Assn.*, editorial, September, 1932.
- (8) FINNEY and FINNEY: Resection of the Pancreas. *Ann. Surg.*, 1928, 88, 584.
- (9) ALLEN, BOECK, and JUDD: The Surgical Treatment of Hyperinsulinism. *Jour. Am. Med. Assn.*, 1930, 94, 1116.
- (10) HARRIS, SEALE: Hyperinsulinism and Dysinsulinism. *Endocrinology*, January and February, 1932.
- (11) TEDSTROM, MILO K.: Hypoglycemia and Hyperinsulinism. *Ann. Int. Med.*, February, 1934.
- (12) WEIL, CLARENCE K.: Functional Hyperinsulinism, Epileptiform Convulsions, Accompanying Spontaneous Hypoglycemia. *Int. Clin.*, December, 1932.
- (13) BROWER, A. BLAINE: Hypoglycemia—its Growing Clinical Importance. *Ohio St. Med. Jour.*, February, 1934.
- (14) BRIGGS, J. FRANCIS: Spontaneous Hypoglycemia. *Minn. Med.*, September, 1934.
- (15) JOSLIN: Treatment of Diabetes. Fourth Ed., 1928.
- (16) BOWEN and BECK: Insulin Hypoglycemia. *N. Y. St. Med. Soc.*, May, 1925.
- (17) JOHNS, H. J.: Lack of Uniformity in Insulin Reaction. *Am. Jour. Med. Sci.*, 1926, 172, 96.
- (18) HARRIS, SEALE: Hyperinsulinism: A Definite Disease Entity. *Jour. Am. Med. Assn.*, Dec. 16, 1933.
- (19) DESJARDINS, A. U.: Action of Roentgen Rays and Radium on the Intestinal Tract. *Am. Jour. Roentgenol. and Rad. Ther.*, September, 1931.
- (20) POWELL, E.: The Role of Diet in the Etiology and Treatment of Mental Disorders Resulting from Hyperinsulinism. *Tri-St. Med. Jour.*, July, 1934.
- (21) HARRIS, SEALE: Epilepsy and Narcolepsy Associated with Hyperinsulinism. *Jour. Am. Med. Assn.*, Feb. 4, 1933.
- (22) Idem: Clinical Types of Hyperinsulinism. *Am. Jour. Digest. Dis. and Nutr.*, October, 1934.
- (23) PATTERSON, J. C., and ELLIOTT, W. G.: Dysinsulinism: Report of Case Treated Surgically. *Jour. Med. Assn. Georgia*, November, 1934.

EXPERIENCES IN THE IRRADIATION TREATMENT OF HYPERTHYROIDISM¹

By S. PAUL PERRY, M.D., *Chicago*

From the Division of Roentgenology, Department of Medicine, University of Chicago

INTRODUCTION

IN THE University of Chicago Clinics the great majority of cases of hyperthyroidism are treated surgically, and irradiation is employed only in post-operative recurrences or in cases in which, for some reason, operation cannot be performed. This paper is a report of the immediate results obtained by irradiation in the latter two categories of cases.

Menville's nation-wide survey of 1932 includes 10,541 cases of hyperthyroidism which had been treated by irradiation. Of these, 66 per cent were listed as cures, 21 per cent showed marked improvement, and 12 per cent failed to respond. Pfahler and Christie have reported a much higher incidence of favorable responses.

There is a great variation in the technical factors employed. Voltage has ranged from 125 K.V. to 200 K.V.; minute intensity from 5 r per minute to 30 r per minute, and total intensity from 500 r to 1,800 r, administered to one large portal or each of several smaller portals. In spite of these technical differences there is a rather striking uniformity in the clinical response. This implies that maximum response is possible by small doses of x-ray and is independent of wave length over a wide range. There seems to be no essential difference between the results obtained by radium or by x-rays. A choice between the two depends upon the type of facilities available.

The relative value of irradiation therapy and surgery in the treatment of hyperthyroidism is still subject to debate. A final decision will be hastened if surgeons and radiologists will forego prejudice and develop self-criticism, emphasizing their own failures rather than their successes.

Of special value would be clinical studies of individual cases that did not respond to one of these forms of treatment but were benefited by the other.

It is beyond the scope of this report to review in detail the literature on the surgical and radiological treatment of hyperthyroidism. Suffice to state that one form or the other may, on the basis of reports published by leading surgeons and radiologists, be justified as the treatment of choice. For example, DaCosta reports that the surgical statistics usually show about 90 per cent rate of "cures," while practically equal percentages of "cures" are reported for irradiation therapy by Pfahler and Christie.

As regards surgical mortality, Richter reports 0.89 per cent in 1,200 cases, and Crile 0.84 per cent in 5,000 cases. The average surgical mortality is perhaps more correctly stated as between 3 and 4 per cent. In this respect, irradiation would seem to have an advantage since its mortality is negligible. However, such low mortality ascribed to irradiation may be due to the fact that the amount of irradiation given is generally regarded as innocuous in so far as danger to life is concerned, and any fatality occurring during the period of treatment is ascribed to the patient's disease rather than to the method of treatment.

The usual surgical treatment entails enforced bed rest for a period of from two to four weeks, whereas the treatment by irradiation is an ambulatory one and the patient need have but very little interruption of his normal daily activity. It will be objected by some that irradiation therapy is very time-consuming and that the patient will be subnormal for long periods. In our experience the patient usually shows definite improvement within a month's time following the beginning of

¹ Presented before the Radiological Society of North America, at the Twentieth Annual Meeting, in Memphis, Tenn., Dec. 3-7, 1934.

treatment, and usually it does not require more than two or three months to attain the maximum beneficial effect.

Response to irradiation appears to be independent of the pathologic type of the goiter. Pfahler is convinced that irradiation does not increase the tendency to malignant degeneration.

ANIMAL EXPERIMENTS

In experiments conducted on dogs, Walter, Anson, and Ivy have shown that clinical doses of irradiation do not alter the histology of the normal thyroid gland. Fibrosis occurs only when intensity is so great as to cause ulceration of the overlying skin, and when it does occur it is confined largely to the capsule of the gland. Experimental hyperthyroidism produced in opossums by Bensley's method of high protein feeding can be prevented by irradiating the animals either before or during the feeding period. This experiment suggests a useful field for irradiation in the post-operative management of hyperthyroidism. There are no clinical studies available on such a procedure.

PRESENTATION OF CLINICAL MATERIAL

Twenty-eight patients have been irradiated in the University of Chicago Clinics in the past two years. Since the follow-up

period on the majority of them is short, results will be considered only in the light of immediate response. For all of these patients the technical factors were the same: 200 K.V., 25 ma., 1 mm. Cu and 1 mm. Al filtration, and 50 cm. focal skin distance. Most patients were treated using three portals: two 10 × 12 cm. portals, one to each lobe of the thyroid, and a 10 × 10 cm. portal over the upper mediastinum. Two treatments of 300 r each (measured in air) were given to each portal, treating one portal daily for a total of six days. However, in one instance tracheal irritation was produced and, following this, treatments were given to one large field, 15 × 15 cm., which included all of the neck and upper mediastinum. Three treatments of 200 r each, given on successive days to this one portal, are considered a series. This series is not repeated in less than a month but is repeated on successive months until the desired effect is accomplished.

Of the 28 cases treated, 17 are now definitely without clinical manifestations of hyperthyroidism, four have been very definitely improved, and seven failed to respond favorably to the treatment. Seventeen of the patients were suffering from post-operative recurrence of hyperthyroidism; 11 had not been operated upon. In addition to the patients' subjective statements, our criteria of improvement have included the following: (1) the basal

TABLE I.—SHOWING THE EFFECT OF IRRADIATION ON 11 PRIMARY CASES

Patient	B.M.R.		Pulse		Blood Pressure		Weight (kg.)		"Cured"	Improved	Failure
	Before	After	Before	After	Before	After	Before	After			
L. H.	+48	+15	99	85	116/66	114/72	54.9	65.1		x	
A. D.	+30	+15	98	93	152/88	140/80	59.7	49.8		x	
G. E.	+42	+30	106	109	160/90	130/74	57.3	51.4			x
L. C.*	+44	- 3	93	70	110/68	120/84	56.2	66.0	x		
R. S.	+33	+ 5	96	88	126/58	108/72	56.7	57.6	x		
M. O.	+28	+27	75	91	138/80	140/80	54.7	59.9			x
M. L.	+32	- 3	108	85	110/70	100/70	55.0	56.1	x		
A. M.	+18	+18	95	93	134/70	124/64	52.0	50.2			x
T. M.	+64	+ 9	92	66	156/78	148/80	76.5	84.5	x		
M. R.*	+44	+16	107	93	130/70	140/80	57.0	56.1		x	
A. G.	+40	+28	97	82	156/90	124/70	71.4	72.5			x
Total									4	3	4
Average	+38	+14	97	88	135/75	126/75	59.2	60.8	36%	28%	36%

* Received iodine during and after irradiation.

metabolism; (2) pulse; (3) blood pressure; (4) weight. No patient has been considered cured unless all criteria have shown favorable responses.

Considered as a whole, the group of 28 patients responded to irradiation as follows: basal metabolic rate before irradiation +35, after +9; pulse before irradiation 97, after 79; blood pressure before irradiation 132/76, after 123/75; weight before irradiation 58.5 kg., after 61.8 kg. It will be seen that the metabolic rate was reduced 26 points, the pulse reduced 18 beats per minute, and the pulse pressure reduced 8 mm., while the weight was increased 3.28 kg., or 7.2 pounds.

When reviewed the group of 17 cases considered as "cures" showed the following: B.M.R. before irradiation +32, after -2; pulse before irradiation 99, after 76; weight before irradiation 56.7 kg., after 61.1 kg.; blood pressure before irradiation 130/72, after 119/74. Thus this group showed a drop of 34 points in B.M.R., the pulse was lowered 23 beats per minute, and the average weight gained was 4.4 kg., or 9.6 pounds, while the pulse pressure was reduced 13 millimeters.

The post-operative group, 17 in all, when

reviewed collectively showed the following: B.M.R. before irradiation +31, after +5; pulse before irradiation 97, after 79; blood pressure before irradiation 131/74, after 123/76; weight before irradiation 57.5 kg., after 61.6 kg. Thus the B.M.R. was reduced 26 points, the pulse dropped 18 beats per minute, and the pulse pressure was reduced 10 mm., while there was a gain in weight of 4.1 kg., or 9 pounds. Thirteen of this group are clinically free from symptoms, one is markedly improved, while three failed to receive any benefit from the treatment.

When taken as a whole the group in which no operative procedures had preceded irradiation showed the following: B.M.R. before irradiation +38, after +14; pulse before irradiation 97, after 88; weight before irradiation 59.2 kg., after 60.8 kg.; blood pressure before irradiation 135/70, after 126/75. The B.M.R. was reduced 24 points, the pulse was lowered 9 beats per minute, the pulse pressure was lowered 14 mm., while the weight increased 1.6 kg., or 3.5 pounds. Of this group, four are clinically free from symptoms, three improved, and four unimproved.

TABLE II.—SHOWING THE EFFECT OF IRRADIATION ON 17 CASES OF POST-OPERATIVE RECURRENCE

Patient	B.M.R.		Pulse		Blood Pressure		Weight (kg.)				
	Before	After	Before	After	Before	After	Before	After	"Cured"	Improved	Failure
K. G.	+32	+ 2	96	84	120/88	108/88	54.8	59.2	x		
E. B.	+19	+ 5	80	70	130/84	134/88	64.8	65.9	x		
M. K.	+25	-13	116	73	122/64	110/70	36.1	43.8	x		
M. G.*	+47	+21	93	82	150/98	140/80	63.3	77.4		x	
D. A.	+31	+28	81	90	116/70	126/88	73.6	74.0			x
B. C.	+24	-11	98	60	120/70	106/64	65.9	73.0	x		
G. B.	+24	-12	85	67	128/80	130/74	56.6	58.7	x		
L. C.	+32	+ 8	85	65	150/70	140/80	49.1	51.6	x		
H. L.	+33	+ 4	101	97	170/80	140/82	50.3	63.0	x		
P. Z.†	+44	+36	81	85	146/80	144/84	55.5	61.9			x
G. P.	+20	+ 5	106	91	118/70	120/74	74.3	75.7	x		
R. M.	+38	- 9	123	79	126/80	110/76	56.8	61.3	x		
M. W.	+37	-21	110	80	154/82	116/74	69.2	76.3	x		
A. M.*	+28	- 2	114	79	132/80	116/74	47.6	50.5	x		
S. M.	+19	-14	73	58	120/70	110/60	38.2	40.4	x		
G. S.*	+43	+50	101	98	106/66	120/70	66.0	58.5			x
E. S.	+34	+ 8	110	85	120/64	114/64	55.8	57.3	x		
Total									13	1	3
Average	+31	+ 5	97	79	131/74	123/76	57.5	61.6	76%	6%	18%

* Received iodine during and after irradiation.

† Did not finish treatment.

In comparing these groups it will be readily seen that the best results have been with patients suffering from post-operative recurrence of hyperthyroidism. The percentage of "cures" in this group is 76 while in the primary group it was only 36.

The results obtained in post-operatively recurrent hyperthyroidism treated by irradiation have proved so satisfactory that irradiation is felt to be the treatment of choice under these circumstances and should be considered, all conditions permitting, before re-operation is recommended. On the other hand, although experience in the primary treatment of hyperthyroidism by irradiation is limited, it is believed that irradiation therapy may well be recommended as the primary treatment in cases of mild or even moderately severe hyperthyroidism of long standing in which, for other medical or non-medical reasons, an operation is to be avoided if at all possible.

Lugol's solution was given to four patients. One received it inadvertently, having taken it before coming for irradiation. She continued its use throughout treatment, doing so on her own responsibility. On two other occasions the metabolic rates after treatment had been reduced but not to normal and, as supplementary treatment, small doses of iodine were given for a short time with satisfactory response. The fourth patient to receive iodine was influenced by neither irradiation nor iodine and was later operated upon.

SUMMARY AND CONCLUSIONS

(1) In the literature it is reported that permanent clinical cures of hyperthyroidism in a great majority of large series of

cases may be brought about by irradiation therapy alone.

(2) The question as to whether surgery or irradiation is the primary treatment of choice in hyperthyroidism is not finally settled.

(3) In the small series of cases here presented in which primary irradiation was given because operation was refused or was for medical reasons contra-indicated, the primary results are not comparable with what might be expected from a similar number of patients operated upon.

(4) In certain cases of mild or moderate hyperthyroidism existing for a long period, or in cases in which for certain reasons operation is to be avoided if at all possible, irradiation is indicated. It should be realized, however, that operation may eventually have to be performed.

(5) In the small series of cases presented, results of irradiation in post-operatively recurrent hyperthyroidism have been very gratifying. In this group, irradiation is considered the treatment of choice and well worth trying before re-operation is contemplated.

BIBLIOGRAPHY

- (1) BENSLEY, R. R.: *Am. Jour. Anat.*, 1916, **19**, 16.
- (2) CRILE, GEORGE, and Associates: *Diagnosis and Treatment of Diseases of the Thyroid Gland*. W. B. Saunders Co., 1932, p. 483.
- (3) DaCOSTA: *Modern Surgery*. W. B. Saunders Co., 1925.
- (4) GROOVER, T. A., and CHRISTIE, A. C.: *Roentgen Treatment of Hyperthyroidism*. *RADIOLOGY*, March, 1934, **22**, 275-279.
- (5) MENVILLE, L. J.: *The Radiologic Aspect of Thyrotoxicosis*. *RADIOLOGY*, March, 1932, **18**, 568-575.
- (6) PFAHLER, G. E.: *Irradiation Treatment of Hyperthyroidism*. *Ann. Int. Med.*, January, 1934, **7**, 868.
- (7) RICHTER, H. M.: *The Surgical Treatment of Thyrotoxicosis*. *RADIOLOGY*, March, 1932, **18**, 542-548.
- (8) WALTER, ANSON, and IVY: *The Prevention of Hyperplasia of the Thyroid in the Opossum by X-rays*. *RADIOLOGY*, March, 1932, **18**, 583-586.
- (9) IDEM: *The Effects of X-rays on the Thyroid and Parathyroid Glands*. *RADIOLOGY*, January, 1931, **16**, 52-58.

RADIOTHERAPEUTIC TREATMENT OF HYPERTENSION AND DIABETES¹

By JAMES H. HUTTON, M.D., *Chicago*

HIGH in the list of causes of death, its proportionate toll increasing, stands the group of pathologic conditions summed up as "essential hypertension" and its allied disorders. Fahr (1) calculated that, in 1924, 140,000 deaths in the United States were due to hypertension or its consequences. This was 23 per cent of all deaths of persons over 50 years of age. Its predilection for brain workers and consequently for some of our most able citizens makes it of far-reaching economic and social importance and, among other considerations, makes it paramount among the problems confronting medicine to-day. It is hoped that these considerations offer justification for presenting to you a new theory as to the etiology and treatment of this syndrome and our experience with therapeutic efforts based on this theory.

Briefly, it is believed that essential hypertension is largely a matter of endocrine dysfunction, probably over-activity, and that this activity can be controlled by means of the roentgen ray.

In 1913, Quadrone (2) reported his experience in the treatment of this syndrome by x-raying the adrenals. How far he proceeded along this line or with what results, I do not know. Since that time almost every book written on the subject has mentioned, for the most part very briefly, the possibility that the adrenals or other of the endocrine glands might have some influence in bringing about hypertension. In recent years four surgical procedures have been devised for the treatment of this syndrome, all directed, in part at least, at the adrenals and designed to reduce their functional activity

to a lower level. DeCourcy (3) removes surgically about two-thirds of each adrenal; Crile (4) and Arn (5) have for several years been doing a denervation operation not only for hypertension but also for recurrent hyperthyroidism, peptic ulcer, and neuro-circulatory asthenia. The Mayo Clinic (6 and 32) has published descriptions of resection of the major and minor splanchnic nerves uni- or bilaterally, and of a technic for severing the anterior roots of the spinal nerves from the sixth thoracic to the second lumbar inclusive (7). Publication of these operative technics offers some support for the idea that the adrenals' functional level is important in the production of essential hypertension. Trolow (8) and his associates report some success in the treatment of essential hypertension by the application of diathermy to the adrenals and neighboring structures.

As far as I know, Cushing (9) was the first to call attention to the fact that the pituitary might be responsible in some instances for this syndrome.

For something more than two years the writer, in co-operation with Dr. G. G. Dowdall, Chief Surgeon of the Illinois Central Railroad, and various members of the medical staff of the Illinois Central Hospital, have proceeded on the hypothesis that the pituitary and/or adrenals were responsible for most cases of essential hypertension, and have attempted to relieve them by x-raying these structures. We believe that our results warrant further study on a larger scale.

Specifically, the endocrine theory of essential hypertension is as follows: The pituitary supplies a functional impetus to the adrenals and itself secretes substances affecting the blood pressure: the adrenals exercise a direct effect on the pressure level. Both the adrenals and the pituitary

¹ Presented before the Radiological Society of North America, at the Twentieth Annual Meeting, in Memphis, Tenn., Dec. 3-7, 1934.

elaborate substances that tend to raise blood sugar and neutralize the effects of insulin. The pathologic state appears when some dysfunction of either or both glands occurs. This dysfunction is considered likely to be a hyperfunction; at least the roentgen-ray application herein described was given at first with that idea in mind. But, while we are reporting a measure of success in a large majority of the cases treated, we are not in a position to declare ourselves positively regarding the exact process of the relief obtained.

For this reason it is difficult also to bring objective evidence, other than that of the sphygmomanometer, to support the claim to relief of hypertension. And sometimes the reading does not appear to be substantially reduced, despite the patient's insistence that he is better. Nevertheless, the subjective evidence of the patient's self-reported improvement in the sense of well-being and relief from headache, tinnitus, vertigo, and other symptoms may properly be given some credence since they are almost constant following this treatment, despite widely varying conditions of physical and mental states.

THE DATA ON WHICH THIS THEORY IS BASED

The Pituitary Body.—The influence exerted by the pituitary on adrenal development and function is rather well established and generally accepted. Our knowledge is based on the degeneration of the adrenals after hypophysectomy, the repair of this degeneration after pituitary transplants, and on the studies of Evans (10), Collip (11), and others, who have extracted an adrenotropic substance from the anterior lobe of the pituitary. Other considerations are as follows:

The adrenal enlargement (usually with hypertension) sometimes found in acromegaly with acidophilic pituitary tumor.

The secondary adrenal hyperplasia occurring in the Cushing syndrome, which he traces to a basophilic adenoma of the pituitary and the hypertension which is a constant of that syndrome.

The work of Moehlig and Osius (12),

who fed animals a high fat diet, with daily pituitrin injections, and produced a pronounced arteriosclerosis and marked hyperplasia of the adrenal cortex within 100 days.

Cushing's (9) observation that all known primary pituitary disorders cause marked secondary changes in the adrenal cortex.

The extremely low blood pressure which is characteristic of Simmonds' disease, a condition generally accredited to almost complete functional breakdown of the anterior lobe, in which adrenal deterioration is part of the general picture.

Moehlig and Bates (13) say:

"Kraus and Traube examined 232 pituitaries of persons who had been ill but a short time, so that no change in the pituitary would be expected from the illness. Another group was obtained from persons who had either died by accident or had committed suicide."

Among the conclusions were the following:

"Normal persons of hypersthenic habitus show, as a rule, a marked increase of the basophil cells as compared with those of the healthy mesosthenic habitus.

"Persons with diseases which attack, as a rule, the hypersthenic type, such as essential hypertension, vascular sclerosis, contracted kidneys, constitutional obesity, and, in a certain degree, chronic alcoholism, progressive paralysis, and aortitis of syphilitic origin, show a very high percentage of basophil cells and a marked increase of the basophil cells as compared with the mesosthenic type.

"Persons with high blood pressure, chronic nephritis, and so-called secondary contracted kidneys also have a marked increase of the basophil cells as compared with the normal mesosthenic type.

"Asthenic persons, such as the diabetic and the tuberculous types in whom the blood pressure is low, show a diminution of the basophil cells in a majority of cases.

"As to the relationship between the basophil cells of the pituitary and the suprarenals, 72.7 per cent of the persons with suprarenals rich in lipid (12 gm. or more) show a marked increase of the basophil cells.

"Our studies on these 232 pituitaries taken from normal and sick persons permit the conclusion that there is a definite relationship between the basophil cells of the pituitary and the constitutional type of the patient; likewise between these and the blood pressure as

well as the state of the suprarenals. In other words, there is a definite relationship between the basophil cells, the constitutional make-up of the patient, the blood pressure, and the size of the suprarenals.

"There is, apparently, also a relationship between the basophil cells of the pituitary, the cholesterol content of the blood, and the suprarenals. This is important because of the relationship between the cholesterol content of the blood and vascular disturbances."

Dr. J. D. Kirshbaum (14) has told me of six cases observed in Dr. Jaffe's laboratory at the Cook County Hospital. Three cases of uremia, two cases of hypertension, and one of hypertension plus diabetes revealed an increase in the number of basophil cells in the anterior lobe of the hypophysis.

Cushing (15) recently reported the finding of a heavy infiltration of basophilic elements in the posterior lobes of six out of nine pituitary bodies from fatal cases of eclampsia, and in some glands from cases of essential or nephrovascular hypertension. He concluded that the source of these hypertensive disorders lies in the posterior lobe of the pituitary body.

The pharmacodynamic effects of pituitrin, many of which depend on its vasoconstrictor and vasopressor properties, constitute the direct influence exerted by the posterior lobe of the pituitary on the blood pressure. Exactly how the basophilic adenoma or hyperplasia brings about hypertension is not well understood.

The Adrenals.—Adrenalin has long been recognized as having a definite effect on blood pressure and blood sugar. The increase in blood pressure and blood sugar resulting from sudden strain, excitement, fright, and exertion of any sort, is likewise to be ascribed, by Cannon's theory of adrenal function, to the outpouring of adrenalin into the blood stream.

There are numerous other supporting data. Of note is Goldzieher's (16-a) observation on adrenal tumors and their relation to blood pressure. He says:

"In brief the writer claims that Volhard's arterial spasm or Munk's undefined 'hematogenous' hypertension is nothing else but a

symptom of over-activity of pressor endocrines and particularly of the phaeochrome system. I wish to state emphatically that I do not identify hypertension with mere hyperadrenalinemia, although adrenalin is the most powerful of the physiological pressor substances. There are other pressor hormones to be reckoned with, such as those of the pituitary and thyroid."

Another item is the frequency, as noted also by Goldzieher (16-b), with which various symptoms of increased sympathetic tonus, such as hyperglycemia, decreased glucose tolerance, and glycosuria, are associated with hypertension. Taken in consideration with the known effect of adrenalin in heightening sympathetic tension, this is, at least, suggestive.

The material here summarized has been collected and printed at length in the writer's three previous publications on this subject (17, 18, and 19).

Assuming the dependability of this assumed concatenation of pituitary influence on the adrenals and other endocrines, on blood pressure and blood sugar, and of adrenal influence on the blood pressure and blood sugar, it is possible to understand how a chronic or persisting pituitary-plus-adrenal over-activity or dysfunction could produce the state we call "essential hypertension," combined with various other symptoms, all possibly more or less dependent on the increased arterial tension. And it is obvious that an attack on the excessive or disordered activity of these two structures should be made in the effort to relieve the patient. It is on that basis that the application of roentgen ray to the pituitary and adrenals is suggested.

The question of why the pituitary and the adrenals should indulge in a disturbed or hyperfunctional activity in middle life cannot be definitely answered, but there are grounds for urging investigation of the possibility that a decline of the sex hormone supply is an important factor. For instance, essential hypertension is most frequent at about the period of the decline of potency. It is a common accompaniment of the menopause and is probably as often associated with sexual deterioration

in the male, although this phase is not usually investigated. (We have noted sexual impotence in a number of young men victims of essential hypertension, but this is by no means a constant finding.)

Alvarez (20) notes:

"It is suggestive also that in young women, there seems to be a high degree of correlation between the incidence of hypertension and the presence of the various symptoms and signs of ovarian hypofunction. It would seem that the internal secretion of the ovary is able in some way to suppress the tendency to hypertension which many of the girls presumably inherit equally with the men."

Goldzieher (16-c) adds:

"The relation between the climacterium in women and hypertension is also striking and many theories have been built up on the conception that functional disturbances of the ovary and hypertension are closely connected. The frequency of hypertension in artificially sterilized women is particularly noteworthy and so is the coincidence of myoma and hypertension."

Fluhmann (21) found an excess of the anterior pituitary sex hormone in women past the menopause. More than ten years ago Mara \tilde{n} on (22) noted his opinion that the adrenals take on added activity at the menopause.

Behind this association of hypertension and lowered flow of gonadal hormones lies the fairly well established idea that the internal secretions of ovary or testicle tend to suppress or balance pituitary function. Supporting this idea are the following:

(1) The inhibition of the growth impetus and closure of epiphyses when the gonadal function develops at puberty.

(2) The scarcely repressed growth of long bones, with resulting eunuchoid proportions, occurring in pre-puberal castrates or individuals in whom genital development does not occur because of disease, injury, or other causes.

Barnes, Regan, and Nelson (23) believed that the ovarian hormone could suppress pituitary activity. They apparently demonstrated the correctness of their idea by showing that female dogs to which

amniotin had been administered experienced only mild diabetes following pancreatectomy. When the injections of amniotin were discontinued, the animals became severely diabetic. Resumption of the injections was followed by a reduction in the severity of the diabetes.

This idea of an endocrine dyscrasia as the cause of essential hypertension is not novel nor entirely original. Quadrone's publication has been referred to and Hofbauer (24) suggested roentgen irradiation of the pituitary in hypertension more than 10 years ago, but did not use the treatment. The adrenal-denervation operations already mentioned, Alvarez' ideas quoted above, the French reports (25 and 26) of adrenal irradiation in hypertension, taken together, indicate that experienced physicians have had the germ of the idea in their minds for an appreciable time, but comparatively little seems to have been done about it. It has been our experience that, the more study and thought one gives it, the more inescapable and the more cogent it becomes. That it needs study there is no denying, but neither is it possible to maintain that it is not worth study. The physiology of the phenomena on which we are reporting is not at all satisfactorily explained—we have made it clear, certainly, that the foregoing observations are only tentative—and much work remains to be done in that phase. This task, however, is beyond the time and facilities available to the present writer: this report is concerned with facts accumulated in the course of active private practice, where the prime and immediate necessity was to relieve the patient of his complaints.

Before passing to a description of the work we have been doing, it seems important to call attention again to the gradually emerging idea of the paramount importance of the pituitary body in many of the physiologic problems confronting medicine. This is especially true of the anterior lobe, where growth, sex, adrenergic, thyrotropic, lactogenic, and diabetogenic principles have been rather defi-

nately identified. Houssay's work (27), repeated by Barnes (28) in Chicago, on pancreatectomized and hypophysectomized dogs, is an important beginning in this study, and it is sincerely to be hoped that this whole problem of pituitary physiology and its ramifications will soon be traced down for us. Of its tremendous and far-reaching importance there can no longer be any doubt. The idea of hypophyseal and adrenal dysfunction utilized in this work is applicable to Graves' disease and diabetes mellitus. We have, in fact, irradiated pituitary and adrenals in a few cases of diabetes and in some of hypertension and diabetes combined, with some success. Our experience in the treatment of diabetes mellitus with the x-ray gives hope that we shall eventually be able to control a great many cases by this means.

To date roentgen irradiation of pituitary and adrenals has been given to 123 patients who were victims of hypertension, and to 12 others who had both diabetes and hypertension.

Of the 123 hypertensives, seven could not be traced, 20 were unimproved, and 96 were definitely relieved, that is, freed of complaints and with blood pressure reduced. Some of the 20 unimproved had what we considered an insufficient amount of treatment, discontinuing on their own responsibility despite blood pressure reduction. A few were dropped after trial had indicated that they were not favorable candidates. Those are the figures; the percentage of improvement is 78.05.

The complaints referred to as relieved were mainly: headache, vertigo, tinnitus, precordial pain, dyspnea, and lack of endurance. Headache has been relieved in practically every instance. Precordial distress has, oddly enough, not been mentioned by the patient in a number of cases until its disappearance was noted after several treatments. This is also true of "heart-consciousness." Vertigo and tinnitus are usually associated with the headache in the patient's story and seem to disappear as the headache goes. Perhaps the most spectacular and (to the patient)

the most satisfying result of treatment is the increased physical endurance most of them experience after a few treatments; they boast of it spontaneously and add that they are "more clear-headed" and can work better.

The response of blood pressure to x-ray treatment varies. In some cases in which there is a marked fall after the first treatment, there is usually a rise of several points but not to the original level. Under further treatment there is another reduction in blood pressure, but usually several treatments are required to bring it to the point obtained after the first. Some cases show no response (occasionally a rise) after each of several treatments and then experience a considerable drop on further treatments. In others the blood pressure appears to rise for about 72 hours after treatment and then declines considerably.

There is no question but that the symptomatic relief of patients is much more striking than the reduction in their blood pressure, in fact, a number have been almost completely relieved of their symptoms before they experienced any marked reduction in blood pressure. In some cases the blood pressure declines satisfactorily and then later rises, but without return of other symptoms. This raises the question as to whether the factor which causes the symptoms may not be distinct from that which is responsible for the abnormal blood pressure.

In some cases discomfort or headache follows treatment to the pituitary, particularly when a heavy dose is used; in such cases the headache is relieved by treating the adrenals, the interrelationship of these two organs being very close. We cannot decide in most cases which symptoms are due to pituitary dysfunction and which to the adrenals. Moehlig (13) notes in this connection as follows: "Primary disease of the suprarenal cortex.... is accompanied by a variable, but, nevertheless, definite, secondary change in the pituitary." And Cushing's observation that secondary adrenal changes are in-

variable in primary pituitary diseases has already been cited.

By way of illustration, we append here summaries of our experience with some typical patients.

Case 1. Mrs. F., aged 51 years, stated that she had known of her hypertension for six years. She was short of breath, tired easily, had a little vertigo, and lately had had some trouble with her eyes, the nature of which she did not understand. Her blood pressure was 170/105; pulse 90. A physical examination revealed the following: the heart was slightly enlarged to the left, but regular; no murmurs were heard; the tonsils were hypertrophied and appeared to be infected; the linea over the lower abdomen were quite marked; the fundi appeared normal. She had had a hysterectomy ten years before for fibroids. Her mother had died of a "stroke" and her father of "dropsy." Her brothers and sisters were free from hypertension as far as she knew. The basal metabolic rate was plus 11. Urine showed an occasional trace of albumen, but was otherwise negative. The total nitrogen was 7.9 grams per 24 hours. Blood count showed: hemoglobin, 90-95; red blood count 4,980,000; white blood count, 8,850; lymphocytes, 44 per cent, polymorphonuclears, 56 per cent. Blood chemistry showed: non-protein nitrogen, 18.4; uric acid, 2.01, and sugar, 60.1. The glucose tolerance was

not done. Phenolsulphonephthalein test returned 60 per cent of the dye in one hour. Under amyl nitrite the blood pressure dropped to 164/102. After two x-ray treatments the blood pressure was 130/80; pulse, 60. Precordial pain, which she did not mention at her first visit, she said had disappeared. She explained that she tired much less easily than when treatment was instituted.

Case 2. Mr. A., aged 40 years, height 6 feet, weight 197.5 pounds, had known of his hypertension for 12 years. The highest reported reading was 250/150. He had had precordial pain for 18 months and had been sexually impotent for two years. He had always been a hard worker and worried a great deal. Two months before I saw him, he had had a left splanchnic nerve resection with little or no relief. When he first came under observation, Sept. 14, 1934, his blood pressure was 184/130. The heart was slightly enlarged to the left but was regular. B.M.R. was minus 13. Blood count showed: H.B., 90; R.B.C., 4,920,000; W.B.C., 7,100; lymphocytes, 25 per cent; polymorphonuclears, 75 per cent. Blood chemistry showed: N.P.N., 26.3; uric acid, 3.1; calcium, 7.2, and sugar, 91.7. Urine was entirely negative; specific gravity, 1.022; no sugar, albumen, or casts. The glucose tolerance test showed: fasting sugar, 91.7, $\frac{1}{2}$ hr. after 100 grams of glucose; 122.8, $1\frac{1}{2}$ hrs.

TABLE I

Sex	Age	Blood pressure before	No. of treatments	Blood pressure afterward	Remarks
M	41	190/125	7	150/98	Headache relieved; strength and endurance improved.
M	53	210/120	5	140/90	Marked improvement; returned to duty after being laid off 1 yr. because of high blood pressure.
M	58	210/150	9	158/120	Headache and vertigo relieved; vision improved.
M	69	190/150		145/90	Headache and dyspnea relieved.
M	52	230/130	12	178/92	Headache and precordial distress relieved; more strength and endurance.
F	53	190/110	4	140/80	Headache and choking spells relieved.
F	55	230/130	5	165/88	Precordial distress, headache, and dyspnea relieved.
M	40	184/130	6	150/110	More endurance; less precordial distress.
F	51	170/105	3	130/80	More endurance; no precordial pain; no shortness of breath, and feels fine.
M	67	225/140	5	155/110	Headache disappeared; no vertigo.
M	53	190/100	2	150/80	Is more relaxed and clear-headed; has more endurance; precordial distress relieved.
F	46	170/100	4	135/90	Feels better; sleeps better, and is less nervous and irritable.

after glucose 161, and $2\frac{1}{2}$ hrs. after glucose, 109.8. After three treatments his blood pressure dropped to 165/120. He reported less precordial distress and more endurance, and a peculiar ashy gray color had been replaced by a normal appearance. Nov. 9, 1934, his blood pressure was 158/108.

In Table I are presented a few cases chosen more or less at random to illustrate the varied response to this form of therapeutic effort.

In some instances patients have been regarded as unimproved but were later found to have experienced a satisfactory reduction in blood pressure without further treatment. An example of this is Mrs. E., aged 52 years, who came under observation in November, 1931. She complained of hot flashes and "rheumatism" of her knees and legs. She said she had slowed down both mentally and physically and had gained 20 pounds in weight in the preceding year. Her B.M.R. was reported as minus 20. She was 5 ft. 9.5 in. in height and weighed 204.5 pounds. Her blood pressure was 165/108. Under treatment she lost weight slowly so that by June, 1932, she weighed 170.5 pounds; her blood pressure was 170/90. In January, 1933, her blood pressure was 178/100. In November, 1933, her weight was 179.5 pounds, and her blood pressure 160/95.

weight was 183.5 pounds. She had no further treatment. On July 26, 1934, her weight was 183.5 pounds; her blood pressure 145/86. Her hot flashes, of which she had complained rather bitterly, were much less troublesome and she stated that generally she felt very well.

We have seen 12 cases of co-existing diabetes mellitus and hypertension, out of which number, nine were men and three were women. Five were greatly improved or completely relieved of both conditions, that is, the glycosuria disappeared and blood sugar was reduced to normal. The blood pressures were as follows:

Before treatment	After treatment	Patient's age	Patient's sex
260/160	150/80	63	F
215/80	138/65	27	M
252/145	140/80	54	M
200/105	140/85	68	M
170/100	150/90	67	F

In two cases only the hypertension was relieved; the diabetes was not materially affected.

Before treatment	After treatment	Patient's age	Patient's sex
160/90	140/80	46	M
195/100	160/90	84	F

In one case the carbohydrate tolerance was improved and the subjective symptoms of vertigo, headache, and weakness almost entirely disappeared, while the blood pressure was reduced but little. One case experienced a reduction of 70 points on the systolic and 60 on the dias-

<i>First Technic</i>								
	K.V.	Port.	Filter	S.T.D.	Ma.	Time	M.A.M.	
Pit.	110	10 × 10 cm.	1 mm. Al 0.25 mm. Cu	50 cm.	4	20 min.	80	
Adr.	Same dosage in every respect							
<i>Second Technic</i>								
	K.V.	Port.	Filter	S.T.D.	Ma.	Time	M.A.M.	r units
Pit.	110	10 × 10 cm.	2 mm. Al	50 cm.	4	7 min.	28	51.8
Adr.	110	20 × 20 cm.	2 mm. Al	50 cm.	4	7 min.	28	51.8
<i>Third Technic</i>								
	K.V.	Port.	Filter	S.T.D.	Ma.	Time	M.A.M.	r units
Pit.	120	10 × 10 cm.	2 mm. Al	50 cm.	5	8 min.	40	106.4
Adr.	120	15 × 15 cm.	2 mm. Al	50 cm.	5	10 min.	50	133

She was given x-ray treatment to the adrenals and pituitary. This treatment was repeated Dec. 14, 1933, and Feb. 8, 1934. At which time her blood pressure was 168/95, B.M.R. minus 20, and her

tolic; improvement in her diabetes did not occur until several months later. One case had only one treatment.

Technic.—Our first consideration was to be sure that no harm was done the patient

by the treatment. Consequently we began with very small doses, the factors being as shown on page 336.

Later, having had the feeling that if still heavier doses were given the results might be obtained more promptly and would be generally improved, we set up the following three sets:

10 × 10 cm. fields to the pituitary from each side

10 × 15 cm. posterior field to the adrenals.

Six hundred r units were administered to the pituitary from each side and 600 r units to the adrenals by the posterior field

<i>Light</i>								
	K.V.	Port.	Filter	S.T.D.	Ma.	Time	M.A.M.	r units
Pit.	130	10 × 10 cm.	2 mm. Al	50 cm.	5	10 min.	50	65
Adr.	130	15 × 15 cm.	2 mm. Al	50 cm.	5	10 min.	50	65
<i>Medium</i>								
	K.V.	Port.	Filter	S.T.D.	Ma.	Time	M.A.M.	r units
Pit.	180	10 × 10 cm.	0.25 mm. Cu	50 cm.	5	10 min.	50	95
Adr.	180	15 × 15 cm.	1 mm. Al	50 cm.	5	10 min.	50	95
			Same	50 cm.				
<i>Heavy</i>								
	K.V.	Port.	Filter	S.T.D.	Ma.	Time	M.A.M.	r units
Pit.	180	10 × 10 cm.	1 mm. Al	50 cm.	5	15 min.	75	142.5
Adr.	180	15 × 15 cm.	0.25 mm. Cu	50 cm.	5	20 min.	100	190
			Same	50 cm.				

However, after using the higher dosage in a few cases, we came to the conclusion that not only were our results not improved but they were definitely not so good as those obtained with the lighter doses. Patients experienced some unpleasant reactions in the shape of headaches, dizziness, and occasionally nausea, many claiming that they did not feel quite as well for a week after treatment as they did before. Furthermore, there was no commensurate reduction in blood pressure, either in degree or in the promptness in which it came about. We have a feeling, which is by no means supported by adequate evidence, that the heavier treatment tends in some way to fix the blood pressure at the level it was when the treatment was given. The experience of other men who have used very much heavier doses than we have ever done tends to strengthen our belief that the smaller doses are preferable.

We have recently been informed (29) that the following factors have been used in another institution:

200 K.V.P., valve-tube rectification
6 ma.
50 cm. distance
0.5 mm. copper and 4 mm. celluloid filtration

in daily doses of 300 r, the pituitary being treated first and then several weeks later the adrenals: no reduction in blood pressure is said to have followed this treatment.

On the other hand, a letter from a physician tells us that he had administered to his own adrenals the following treatment:

Aperture: 9 × 15 cm. (single aperture for both adrenals)
Target: 50 cm. skin distance
Filter: Copper, 0.75 mm.
Aluminum, 1 mm.
Adrenal at 7.5 cm.
Dose: 30 per cent of 814 r units at the adrenal.

The above was given in two half hourly treatments on successive days. This was said to have been followed by relief of most of the subjective symptoms, particularly headache, with considerable reduction in blood pressure.

On the other hand, Hubeny (29) used the following factors in the treatment of a case to which he gave three treatments:

Kilovolts, 115
Skin target distance, 25 cm.
Filter, 4 mm. aluminum
Milliamperes, 5

Time: 8 minutes to each side of the
pituitary
18 minutes to the adrenals
Pituitary and adrenals treated at one
sitting

The blood pressure continued to decline for several months after treatment was stopped and reached entirely normal levels.

However, it is probably true that this treatment cannot ever be absolutely standardized. In dealing with human beings, the infinite variety every doctor comes to know must always be taken into account and it is our effort to adapt the treatment to the individual after determining his idiosyncrasies rather than to subject him to a pre-conceived idea of what he needs. The variations in roentgen-ray machinery and similar factors must also be considered. The foregoing technical data must therefore be accepted in the light of this need.

Before treatment is instituted, the patient should be given the benefit of a very searching physical examination, in which the state of the kidneys should be carefully investigated. While he is under treatment, he should be carefully supervised; the blood pressure should be taken at least once a week, and the urine should be examined before each treatment.

In our examination a 24-hour specimen of urine is examined. The blood sugar, N.P.N., uric acid and calcium are determined. A phenolsulphonephthalein test is run. We frequently do a B.M.R. and glucose tolerance. The vast majority of patients with essential hypertension exhibit a diabetic type of sugar curve after the ingestion of 100 grams of glucose. (O'Hare (30) suggested many years ago that this test might be used to separate the nephritic from the essential type of hypertension. Those exhibiting the diabetic type of sugar curve, he believed, belonged to the essential variety.)

We have done 47 glucose tolerance tests on 45 patients. Thirty-one of these had a rise of blood sugar to above 170 mg., 21 having a rise to more than 200 mg. of blood sugar and one man had a rise to

333 mg. We do not know what effect treatment has on the glucose tolerance, as we have been able to repeat the test after treatment in only two cases. In both, however, the blood sugar curve was more nearly normal after irradiation.

Cushing (9) noted some osteoporosis in his cases of pituitary basophilism. We thought that perhaps the pituitary activity might be reflected in the parathyroids. However, blood calcium is practically always on the low side of normal. As a matter of fact, readings below 8 mg. per 100 cc. of blood are much commoner than those above 9 mg.

The B.M.R. varies from normal about as often in one direction as the other, however, we have not followed this in enough cases to correlate with response to the irradiation. In those cases that have been followed, the B.M.R. has usually shown a decline, having fallen in one instance from plus 48 to minus 6; in another from plus 10 to minus 6.

It is our belief that Stieglitz (31) is correct in assuming that essential hypertension is first a paroxysmal affair, the rise being due to spasm of the vessels. Later this spasm becomes constant and the tension remains well above normal. This is followed by changes in the vessel walls which are irreversible and fix the pressure more or less permanently at a high point. We believe that the amyl nitrite test furnishes some idea as to that portion of the abnormal blood pressure which is due to spasm. Consequently of late we test every patient to see how much reduction in pressure can be brought about by the inhalation of amyl nitrite. The reduction in blood pressure effected by that means gives us some idea of how much reduction may be expected as the result of irradiation.

Some patients vomit after irradiation; we do not know why this occurs, but have made it a rule not to continue treatment in these cases. We persisted in one or two of these cases at first, but found that they were not being materially benefited and since then have abandoned the irradiation therapy when vomiting occurs.

It is my impression that hypertension occurring in persons of slight build is rather more resistant to treatment and offers a poorer prognosis than that occurring in taller persons and those of a heavier build. This, however, is an impression rather than an established fact.

The skin shows a rather pronounced reaction to these treatments; it tends to become smoother, softer, and more moist. The quality of the nails improves. In at least one instance there has been a rather considerable loss of excess hair on the thighs, which could not be called a case of hirsutism, but the thighs were covered with a rather heavy growth of coarse black hair which extended to the groin. After a few treatments this almost entirely disappeared and the skin which had been abnormally rough became quite smooth and moist. Another patient had a severe generalized psoriasis, the scaling being very troublesome. After the first treatment these scales almost entirely disappeared; the lesions appeared to be more active but none of them have disappeared.

The menstrual periods, if irregular, tend to become regular and the periods more normal as to duration and quantity.

The blood pressure is not always reduced by this treatment. We have a number of diabetics to whom the same factors of treatment have been given without any change in blood pressure but with considerable increase in carbohydrate tolerance. Data at this time tend to support the belief that diabetics will do better on smaller doses of roentgen-ray than are necessary to correct essential hypertension.

Patients coming from families in which many members are victims of hypertension appear to respond favorably to this method of treatment.

We have had a few cases which had a fair amount of treatment with but little improvement. A few others showed a satisfactory response at first, but later the blood pressure rose almost to the original level. One case has shown no response at all. We do not know the reason for these failures.

Undoubtedly the age of the patient and the duration of the hypertension have much to do with the prognosis. The younger the patient, the shorter the duration of his hypertension, the better the outlook. That probably explains why patients coming from our out-patient department have done better than patients in the hospital.

It will be noted that this discussion is concerned with the treatment of essential hypertension, consequently, we did not expect to treat any nephritics with hypertension. However, other men have sent in a few nephritics who have had this treatment, some of which have experienced some symptomatic improvement and reduction in blood pressure. Goldzieher's (16-b) idea regarding the relation of hypertension to nephritis is probably correct in many cases. Such patients might show considerable improvement as a result of this treatment, but certainly it cannot be expected to relieve nephritis. No marked relief should be expected in cases of marked arteriosclerosis, although where the pressure is abnormally high and there is fear of a rupture of some vessel, this treatment might be used to effect reduction in pressure to a safer level. A man 79 years of age and a woman 84, both suffering with general arteriosclerosis, were definitely better following this treatment. In cases in which the sclerosis is pronounced, we believe the patient to be undoubtedly better off if the pressure remains well above the theoretical normal and we do not attempt to reduce it much. Hypertensive heart disease is not a contra-indication and, as a matter of fact, its victims should improve following this treatment. Angina pectoris at this time cannot be regarded as a contra-indication and there is some reason for believing that the attacks may be lessened in frequency and severity by irradiation.

SUMMARY

A previously suggested theory as to the etiology of essential hypertension is expanded and modernized in the light of re-

cent experience in endocrinology. This theory is: That the pituitary body and adrenals, by some spontaneous dysfunction, probably a hyperfunction, set up the abnormal arterial tension.

The evidence supporting the claim of pituitary influence on the adrenals and of direct hypophyseal influence on blood pressure and the claim of adrenal influence on blood pressure is summarized briefly.

A hypothesis that this hyperfunction may be due to withdrawal of the gonadal hormonal factor controlling pituitary activity is set forth, with brief summation of the data supporting it.

The results of attempts to reduce this theorized pituitary-adrenal over-activity by means of roentgen irradiation are described as follows: 96 of 123 patients were definitely improved, including in most cases a reduction of the sphygmomanometer reading and in all cases relief of the distressing associated symptoms. The responses of various symptoms to the treatment are described.

Several typical case histories are presented.

This theory is also applicable to diabetes mellitus, and some notes on a few cases of diabetes and of diabetes plus hypertension are given.

The radiological data are presented.

Sundry notes and observations are included as to the handling of these patients, prognosis, complications such as nephritis, angina pectoris, arteriosclerosis, etc., and the need for careful individualized supervision of these cases is emphasized.

BIBLIOGRAPHY

- (1) FAHR, GEORGE: Hypertension Heart. *Am. Jour. Med. Sci.*, April, 1928, **175**, 453-472.
- (2) QUADRONE, C.: *Riforma Medica*, Feb. 8, 1913, 29.
- (3) DECOURCY, JOSEPH L., DECOURCY, CARROLL, and THUSS, OTTO: Subtotal Bilateral Suprarenal-ectomy for Hypersuprarenalism. *Jour. Am. Med. Assn.*, April 7, 1934, **102**, 1118-1122.
- (4) CRILE, GEORGE W.: Recurrent Hyperthyroidism, Neurocirculatory Asthenia and Peptic Ulcer: Treatment by Operations on the Suprarenal-sympathetic System. *Jour. Am. Med. Assn.*, Nov. 28, 1931, **97**, 1616-1618.
- (5) ARN, E. R.: Personal communication.
- (6) CRAIG, W. MCK., and BROWN, G. E.: Resection of the Splanchnic Nerves in Cases of Hypertension. *Proc. Staff Meet.*, Mayo Clin., June 14, 1933, **8**, 373-376.
- (7) ADSON, ALFRED W., and BROWN, GEORGE E.: Malignant Hypertension: Report of Case Treated by Bilateral Section of Anterior Spinal Nerve Roots from the Sixth Thoracic to the Second Lumbar, Inclusive. *Jour. Am. Med. Assn.*, April 7, 1934, **102**, 1116-1118.
- (8) TROLOW, MALKOWA-RIABOWA, and ALTMANN-PARGMANIK: Local Application of Diathermy in Essential Hypertension. *Wien. klin. Wchnschr.*, Sept. 14, 1934, **47**, 1121.
- (9) CUSHING, HARVEY: The Basophil Adenomas of the Pituitary Body and Their Clinical Manifestations ("Pituitary Basophilism"). *Bull. Johns Hopkins Hosp.*, March, 1932, **50**, 137-195.
- (10) EVANS, HERBERT M.: Present Position of Our Knowledge of Anterior Pituitary Function. *Jour. Am. Med. Assn.*, Aug. 5, 1933, **101**, 425-432.
- (11) COLLIP, J. B., ANDERSON, EVELYN M., and THOMSON, D. L.: Adrenotropic Hormone of Anterior Pituitary Lobe. *Lancet*, Aug. 12, 1933, **2**, 347.
- (12) MOEHLIG, R. C., and OSIUS, E. A.: The Pituitary Factor in Arteriosclerosis: Its Experimental Production in Rabbits. *Ann. Int. Med.*, December, 1930, **4**, 578-591.
- (13) MOEHLIG, R. C., and BATES, G. S.: Influence of the Pituitary Gland on Erythrocyte Formation. *Arch. Int. Med.*, February, 1933, **51**, 207-235.
- (14) KIRSHBAUM, J. D.: Personal communication.
- (15) CUSHING, HARVEY: Hyperactivation of the Neurohypophysis as the Pathological Basis of Eclampsia and Other Hypertensive States. *Am. Jour. Path.*, March, 1934, **10**, 145-175.
- (16) GOLDZIEHER, MAX: The Adrenals. Macmillan Co., New York, 1929, (a) pp. 233-234, (b) pp. 253-254, (c) p. 240.
- (17) HUTTON, JAMES H.: Diabetes Mellitus and Essential Hypertension: A Theory as to Their Etiology and Treatment. *Ill. Med. Jour.*, December, 1933, **64**, 539-547.
- (18) Idem: Experiences in the Treatment of Hypertension with the X-ray. *Ill. Med. Jour.*, August, 1934, **66**, 120-126.
- (19) Idem: X-ray Treatment of Essential Hypertension: A Report of Progress. *Int. Jour. Med. and Surg.*, September, 1934, pp. 343-348.
- (20) ALVAREZ, W. C.: Blood Pressure in 15,000 University Freshmen. *Arch. Int. Med.*, July, 1923, **32**, 17-20.
- (21) FLUHMAN, C. F.: Anterior Pituitary Hormone in the Blood of Women. *Endocrinology*, May-June, 1931, **15**, 177-183.
- (22) MARAÑON, G.: *La Edad Crítica*. Soc. Espan. de Pub. Med., Madrid, 1919.
- (23) BARNES, B. O., REGAN, J. F., and NELSON, W. O.: Improvement in Experimental Diabetes Following the Administration of Amniotin. *Jour. Am. Med. Assn.*, Sept. 16, 1933, **101**, 926, 927.
- (24) HOFBAUER, J.: Personal communication; also *Archiv für Gynäkologie*, 1923, **120**, and 1922, 117.
- (25) Foreign Letters. *Jour. Am. Med. Assn.*, Aug. 27, 1927, **89**, 705.
- (26) VAQUEZ, HENRI, and LAIDLAW, G.: Diseases of the Heart. W. B. Saunders Co., Philadelphia, 1924, pp. 461, 462.
- (27) HOUSSAY, B. A., and BIASOTTI, A.: Hypophysis, Carbohydrate Metabolism and Diabetes. *Endocrinology*, Nov.-Dec., 1931, **15**, 511-523.
- (28) BARNES, B. O., and REGAN, J. F.: Relation of Hypophysis to Experimental Diabetes. *Science*, Feb. 24, 1933, **77**, 214.
- (29) Personal communications.
- (30) O'HARE (mentioned by HERRICK, W. W.):

Hypertension and Hyperglycemia. Jour. Am. Med. Assn., Dec. 8, 1923, 81, 1942-1944.

(31) STIEGLITZ, EDWARD J.: Arterial Hypertension. Paul B. Hoeber, Inc., New York, 1930.

(32) BROWN, GEORGE E.: Sympathectomy for Early Malignant Hypertension. Med. Clin. N. Am., September, 1934, 18, 577-583.

DISCUSSION OF SYMPOSIUM ON DUCTLESS GLANDS

DR. HUTTON (Chicago): Naturally I feel flattered at the compliment of being invited to appear before this group; at the same time, I feel considerable timidity in venturing to discuss a form of therapy in which you are the foremost experts in the world. The only hope I have of "getting by" with it is to adopt the tactics accredited to Gladstone, who was something of a Greek scholar as well as a lawyer. In the presence of lawyers he discussed Greek, and in the presence of Greek scholars he discussed law.

So hoping that you may be somewhat guilty of the fault charged to all specialists—that of limiting yourselves too much to your own specialty—perhaps if I talk about the clinical and internists' side of this we shall get along.

DR. M. J. HUBENY (Chicago): First, I want to make an acknowledgment that I don't know very much about this. On the other hand, I want to express my gratitude for being given the opportunity to work with Dr. Hutton, because there are several things in common between the endocrines and radiant energy. That is, their subtle action and the necessity for the most careful application of these particular remedial measures.

Dr. Hutton has given you the symptomatic conditions, the close observation of the patient, and has given you a variety of technics.

The thing that has impressed me in practically all these papers—and I was very glad that Dr. Perry brought out the thing he did—is, that in spite of the variable methods of treatment, we have a high degree of uniformity in our end-results.

I am not going to say very much about the symptomatic side of it because Dr. Hutton knows so much more about it, and,

as I said before, he does this so thoroughly and so well and with such a great amount of care, realizing that these things are so finely balanced; with improper attention, one can create a much greater imbalance along certain directions than the original disease for which one is treating the patients.

I have been impressed with some of the good end-results and the relatively small doses necessary to produce those results. One of the low voltage technics is something like this: portals about 6 centimeters square, about 16-inch skin-focal distance, 115 K.V., 5 ma., filter of 4 mm. of aluminum, time approximately 8 minutes, which is equivalent to 13.2 r per minute, which gives a total dose of 105.6 r. With these factors, the erythema dose runs to about 400 r.

Just before coming to this assembly, I overheard a discussion in which it was stated that a group of factors in which the voltage was low and produced a certain number of r could be transposed into a formula in which the voltage was higher, the filtration heavier, and the number of r the same as before. This may be true as to the number of r, but it is not true as to the amount of r necessary to produce an erythema; in the lower voltage with less filtration it will take less r to produce an erythema than the formula in which the voltage is higher and filtration is heavier. That brings us back to the old question of the amount of radiation absorbed by the tissues, and this is exceedingly important; it is the biological-chemical effect that is important. I am convinced that we have an additional effect on cells which is undesirable, namely, a mechanical disturbance, such as physical displacements of the cells and their structures, and that this tends to be present in an increasing amount as voltages go up. I am also convinced that the cells have an affinity for a certain amount of radiation, which might be designated as "sensible absorption," and that the lower voltages with relatively small filtration and less homogeneity of the rays, contain sufficient varieties of wave lengths to give the

cells an opportunity of selecting a suitable affinity. Cells are or are not susceptible to x-rays and if not, no method is at present available to make them so. It is almost axiomatic that in diseases in which the x-rays are of proved value, it is not necessary to produce an intentional erythema.

Certain of these cases have produced some interesting phenomena. One case exhibited a temporary alopecia over the treated pituitary areas, not due to the amount of the x-ray. It is well known that hair growth is influenced by the pituitary gland and it is possible that the joint effect of the x-rays on the gland and the skin caused the alopecia.

The possible complexities can be comprehended when it is understood that most physiologists are agreed that the pituitary gland has eight hormones, and that each one has three functions. It is calculated that, because of this, over six thousand combinations are possible. It is impossible to make biopsy studies of the sella, consequently all our conclusions will have to be made on the physiologic end-results. Little reliance can be placed upon the size of the sella—I mean, as far as physiologic disturbance is concerned. Of course, this remark does not refer to those that are definitely enlarged, but only to normals or borderline sizes and contours.

In some of these cases I included the carotid plexus; however, only time will tell us as to the effectiveness and limitations of this method of treatment. No doubt, many of you will come to the meeting next year, extolling its virtues or condemning some of its features, based on your personal experiences and observations; however, it is hoped that many of these cases will come to you before they have been long existent.

Dr. Barrow's paper was very interesting. I have had no similar cases. However, I did treat a patient's head, hoping it might favorably influence attacks of grand mal, and he came in six weeks later with a wonderful crop of boils on which I am now having some blood chemistry tests done. He had a somewhat similar spontaneous attack about sixteen years ago.

DR. R. P. POTTER (Marshfield, Wis.): I wish to congratulate Dr. Barrow on the excellent paper he has presented on the subject of hyperinsulinism, and on the results he has obtained from roentgen therapy. It will be interesting to follow these cases and to observe if they remain well over a period of years.

I have not treated any cases in children or young adults, but should like to report a case of hyperinsulinism in a man over 60 years of age.

At the Radiological Society meeting in Chicago in 1928 I read a paper on intrathoracic tumors, citing a case of a man aged 62, on whom we operated, removing a four and one-half pound fibrosarcoma from the left thoracic cavity in November, 1927. Previous to the operation the man had had attacks of mental confusion and delirium which, I believe, were due to hypoglycemia, but the condition was not recognized as such at that time. Following the removal of the tumor the man made an uneventful recovery, did not have any further attacks of mental confusion, and remained entirely well for six and one-half years, when he again developed attacks of mental confusion, exhaustion, and delirium of serious proportions. These conditions were immediately relieved by intravenous glucose, but he continued to require food or glucose at one and one-half hour intervals. The blood sugar was found to vary from 70 to 30 mg. On giving sugar tolerance tests the blood sugar would rise to 215 mg., and rapidly go down to as low as 30 mg.

X-ray studies of the chest revealed that the left side, which had remained clear for several years, was now nearly filled with a dense mass. Re-examination of the chest at intervals showed the density increasing, until the left side was entirely filled. Suspecting a lesion of the pancreas, adrenals, or pituitary, adrenalin and pituitrin were given when the blood sugar curve was going down, but neither had any effect. A thorough neurologic study failed to point to a lesion in the brain.

We cannot conclude that this man had a tumor of the pancreas seven years ago,

causing hypoglycemia at that time, because he remained well for six and one-half years following the removal of the thoracic tumor and there was no treatment of the pancreas at that time.

We might suspect that he now has a metastasis to the pancreas, since the original tumor that was removed was malignant; however, metastases to the pancreas are not common. Also, this man had previously recovered from a similar attack following the removal of a thoracic tumor. I believe that we are justified in assuming that the hypoglycemia in 1927 was due to the presence of the thoracic tumor and that the hypoglycemia is again due to the presence of the large newgrowth which he now has.

It is said that bronchogenic tumors may produce an insulinoïd substance, and it would appear that such is the case here, and that we are dealing with a case of hyperinsulinism of that type. Concluding that we were dealing with a recurrence of the fibrosarcoma, which was large and not amenable to surgery, and suspecting that the pancreas might also be involved, roentgen therapy was given. Small doses caused anorexia, nausea, and vomiting. However, he received 2,000 r in divided doses to the left side of the thorax and over the pancreas. Some benefit was received as was evidenced by the fact that he was able to go three hours between feedings instead of one and one-half hours as before. Last week [November, 1934], this man developed a rather sudden abdominal distention and died a few hours later.

At autopsy an incarcerated right inguinal hernia was found. The left side of the chest was completely filled with numerous tumor masses of various sizes, fibrous in character, evidently a recurrence of the fibrosarcoma. There was no evidence of gross lesion of the pancreas, adrenals, or of any other organ. Since no lesion of these organs was found, we must conclude that this was a case of hyperinsulinism due to secretion of insulinoïd substance in a bronchogenic tumor. The hyperinsulinism was relieved on removal of the tumor seven

years ago, reappearing again on recurrence of the tumor six and one-half years later. Further evidence is seen from the fact that x-ray therapy, which retarded the growth of the tumor somewhat, had a beneficial effect on the time of recurrence of symptoms of hypoglycemia.

DR. CHARLES F. BAKER (Newark, N. J.): Dr. Hubeny has asked me to tell of our experience with a few cases. We treated two series of ten each: one series received 100 r over each side of the skull and over the adrenal glands. In treating the adrenals we used a large cone directed in the mid-line and including both kidney areas. The second series received 100 r to one carotid sinus. We seemed to get about equal benefit with either method—about 50 per cent were improved. We seemed, however, to feel that better results were obtained in those patients in which the treatments were given over the pituitary and adrenal glands.

DR. BARROW (closing): I do not know that I have anything to say further than to report that the two cases which I had not time to present were, one, practically a duplicate of that I did present, and the other, a case of what is ordinarily termed epilepsy.

I do not know but that, in giving these doses supposedly to the pancreas, I am giving what is sometimes spoken of as a "stimulative dose" to the adrenals. Possibly so; I do not know.

The cases are reported simply because of the fact that for over a year we have had a symptomatic cure without any alterations in treatment otherwise.

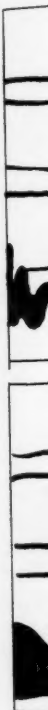
DR. PERRY (closing): Dr. Hubeny has asked about our technic: we use 200 K.V., 25 ma., and a filter of 1 mm. of copper plus 1 mm. of aluminum. We are convinced that there is no specific relationship between wave length and biologic effect, and prefer this relatively high voltage and heavy filtration simply because it allows a rather uniform irradiation of the whole

area under treatment. As we see it, the only possible advantage of a less penetrating beam would be the sparing of normal tissue beneath the thyroid, because we hold, with Landauer, that there is no such thing as shooting through tissue nearer the surface without affecting it.

The question has been raised as to the

dependability of the surgical statistics I have quoted. I believe that the very mass of them makes them dependable. There is unevenness, of course, and one must use discretion, but most of us know which surgical writers to turn to for statistics of this sort.

HO
ing
port
I am
comm
with I



Fi
show
flexu
was s
Fi
enem
bari
the
(Aug
mad

searc
rece
not f
1 P
Amer
phis,

BILIARY COLIC FISTULA¹

By H. B. PODLASKY, M.D., *Milwaukee, Wis.*

HOPE I am not presumptuous in assuming that I am the second observer to report a case of this type. In this statement I am borne out somewhat by a personal communication from Dr. Firor, associated with Dr. Waters, who made a thorough

A case of biliary colic fistula is reported because of the fact that it presents a condition which is rarely diagnosed by roentgen methods before operation. In the roentgen literature there appears only one other reference, namely, that of Judd and Bur-

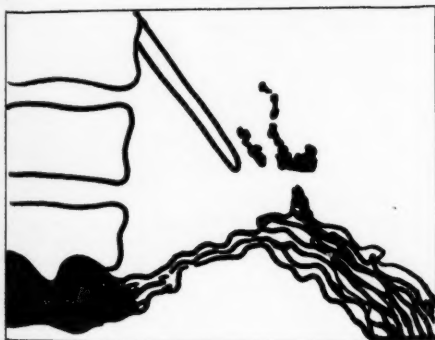
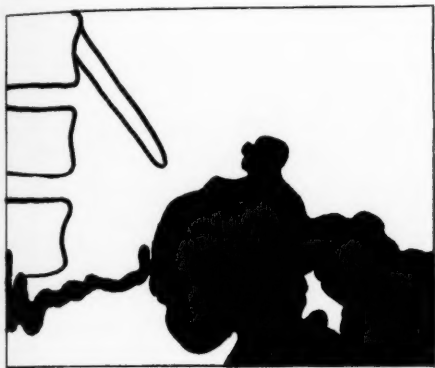


Fig. 1 (*above*). Six-hour film; ingested barium showing in gall bladder continuous with hepatic flexure (Aug. 24, 1932). (Diagram from which slide was made.)

Fig. 2 (*below*). After evacuation of barium enema, hepatic flexure of the colon is shown with barium lining the mucosa. Immediately above the colon is barium shadow in the gall bladder (Aug. 27, 1932). (Diagram from which slide was made.)

search of the literature up to 1933, and who recently stated that since that time he has not found a similar case reported.

¹ Presented before the Radiological Society of North America at the Twentieth Annual Meeting, at Memphis, Tenn., Dec. 3-7, 1935.

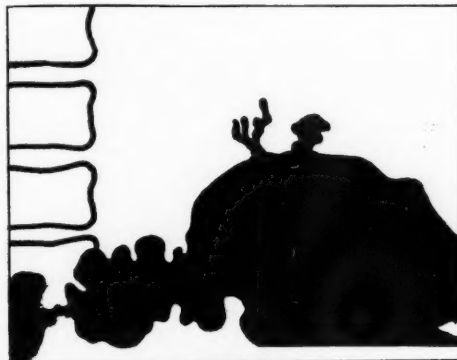


Fig. 3 (*above*). Barium enema filling hepatic flexure of colon and partially filling adjacent gall bladder in an irregular manner (Aug. 27, 1932). (Diagram from which slide was made.)

Fig. 4 (*below*). Fairly large amount of barium escaping from a well-filled hepatic flexure (Aug. 29, 1932).

den, in 1925, calling attention to four cases of this type diagnosed by the roentgen ray.

The case here reported will perhaps prove of interest not only on account of the possibility that it may be the fifth case reported by a second observer after a lapse of almost ten years, but because it

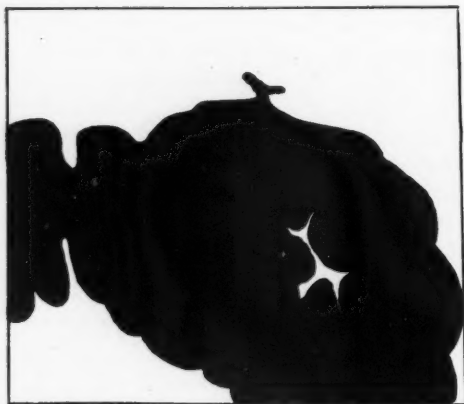


Fig. 5. Distended hepatic flexure, with a very slight escape of barium into gall bladder (Dec. 28, 1932).



Fig. 6. Six-hour film. Hepatic flexure almost empty, barium escaping into gall bladder (Dec. 28, 1932). (Diagram from which slide was made.)

At times both gas and varying amounts of barium may be noted in the filling defect.

Biliary colic fistula should not be confused with the much more commonly visualized biliary duodenal fistula, of which there have been 36 cases reported. A case of this type, namely, biliary duodenal fistula, is also shown to bring out the marked difference in roentgen manifestations. The accompanying illustrations will serve to demonstrate the variability of the roentgen manifestations.²

CASE REPORT

The patient, Mrs. M. R., is a white female, aged 60, who entered the hospital on Sept. 25, 1933, with complaints of

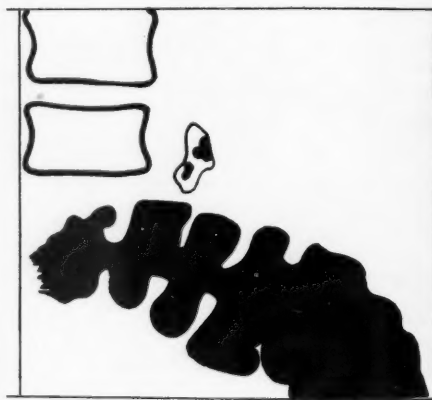


Fig. 7. Six-hour film made on third examination. Gas and barium in gall bladder (Sept. 29, 1933). (Diagram from which slide was made.)

was examined three times—twice in 1932 and once in 1933, just prior to operation. Each examination disclosed the fistulous tract both after the ingested meal and the barium enema series. It was also found on films after the barium enema had been evacuated.

It may be emphasized that in each examination the filling defect as noted immediately adjacent to the hepatic flexure was not duplicated in a single instance. The defect, if it may be so termed, manifested itself either as an air or gas channel or a small or large, very irregular pocket containing barium which had escaped from the colon into the adjacent gall bladder.

vomiting, pain between the shoulder blades, and loss of weight.

History of Present Illness.—She has had attacks of pain and vomiting on and off for the past year. Vomiting relieves the pain. She also has dyspepsia following the ingestion of meat, fried food, and fats. Within the past year there has been a weight loss of 55 pounds, during which period she has been treated at the dispensary. The day before admission to the hospital she vomited and the pain became worse; this was followed by a fainting spell.

² I am indebted to Mr. Leo Massopust, of Marquette University, for the preparation of the diagrams.

Past History.—Pain in the right hypochondrium about fifteen years ago which lasted about two months; treated then by Dr. G. W. Nelson. No history of other illnesses.

Family History.—Father and mother died of old age; five brothers are living and well; two sisters are living and well. There is no family history of carcinoma or tuberculosis.

Examination (by Systems).—C.N.S.: Headaches when seized with pain in right upper quadrant. C.R.S.: No cough, dyspnea, palpitation, or precordial pain. G.I.S.: Appetite fair; constipated for years; uses mineral oil and some "cathartic pills"; no melena, jaundice, or diarrhea. G.U.S.: No dysuria, frequency, or burning. Catamenia: Climacteric fourteen years ago; menses regular previously; no bleeding, spotting, or discharge since menopause.

Social History.—Age 60 years, housewife; seven pregnancies (five children living and well, one child died at two years, one miscarriage).

Physical Examination.—General: Well developed, cachectic old woman. *Head:* Eyes—Pupils react to light and accommodation. Ears and nose—No discharge. Mouth—Plates; no congestion; tongue not coated; pharynx clean. *Neck:* No adenopathy; thyroid not felt. *Chest:* Lungs—Resonant; breath sounds clear; few crepitant râles posteriorly at bases. Heart—No enlargement or arrhythmia; no murmurs; blood pressure, 148/98. *Abdomen:* Soft tissue turgor lost; no palpable masses; no tenderness in epigastrium or gall-bladder region. *Extremities:* No varicosities; no edema. *Reflexes:* Normal.

Laboratory Examination (Sept. 26, 1933).—Red blood count, 3,080,000; hemoglobin, 49.2 per cent; color index, 0.8 per cent; leukocytes, 7,000; polymorphonuclears, 72 per cent; lymphocytes, 26 per cent; monocytes, 2 per cent.

Urine: Specific gravity, 1.018; reaction, acid; albumen, trace; sugar, 0; blood, few red blood cells; cells, 18–20.

Sedimentation rate: Start, 100 per cent;



Fig. 8 (above). Gas outlines of narrow tracts immediately adjacent to colon (Sept. 29, 1933). (Diagram from which slide was made.)



Fig. 9 (below). Colon enema, made during the third examination, showing gas and barium immediately adjacent to hepatic flexure (Sept. 29, 1933).

15 min., 88 per cent; 30 min., 78 per cent; 60 min., 56 per cent; 120 min., 41 per cent; 24 hrs., 30 per cent.

Gastric Analysis (Sept. 27, 1933).—

	Free HCl	Total Acid	Lactic	Blood
15 min. after histamine	0°	Unable	0°	+
30 " " "	0°	because	0°	+
45 " " "	10°	bloody	0°	+

Microscopic: Epithelial cells; 6–8 leukocytes; 25–30 red blood cells; fat droplets.

Feces (Sept. 28, 1933).—Blood, strongly positive.

Blood Cholesterol: Test showed 164.8 mg. on Sept. 26, 1933.

Icteric Index: Was 5.4.

The patient was put at bed rest on ad-

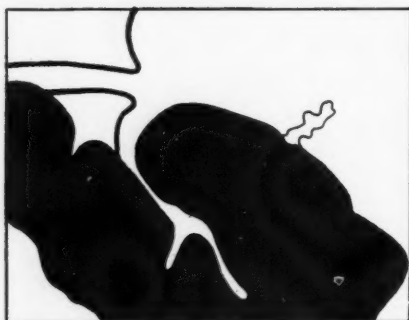
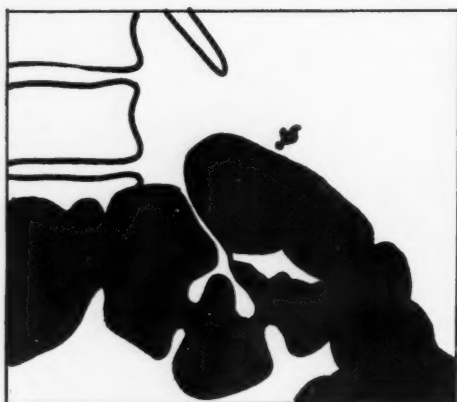


Fig. 10 (above). A very slight amount of barium escaping from colon into gall bladder from barium enema (Sept. 29, 1933).

Fig. 11 (below). Small irregular outline of gas immediately adjacent to colon. Barium enema outlining the colon (Sept. 29, 1933).

mittance. Temperature was 99; pulse, 98; respiration, 28.

She was given supportive treatment consisting of two intravenous injections of 500 c.c. each of 1.8 per cent NaCl and 10 per cent glucose.

On Oct. 5, 1933, she was operated on. A fistulous tract was found between the hepatic flexure of the colon and the fundus of the gall bladder. The bowel was separated from the gall bladder and sutured. The gall bladder contained one large stone, which was removed. The stomach was found free and normal, as were the transverse colon and the liver. A cigarette drain was inserted.

On Oct. 6, 1933, at 6.15 A.M., the patient became restless and irritable. It was impossible to get the pulse or blood pres-

sure. She complained of pain in the left calf and at 7.15 she was pronounced dead.

Pathologic Report.—The gall bladder contains a small calculus. There is a small diverticulum of the fundus. The mucosa of the upper half is irregular and hyperplastic. Microscopic examination shows diffuse glandular hyperplasia of the mucosa; infiltration of the mucosa with lymphocytes. There is no evidence of malignancy. The mucosa is necrotic and ulcerated in places.

Diagnosis.—Chronic interstitial cholecystitis; polypoid hyperplasia of the gall bladder; cholelithiasis.

Films and lantern slides of a case with a biliary duodenal fistula were shown in the exhibit at Memphis, in December, 1934.

INTERNAL BILIARY FISTULAS

Of the forty-odd cases reported in the roentgen literature, most of them have been biliary-duodenal fistulas. Only four cases have been reported in the roentgen literature of connection between the colon and gall bladder. The forty cases are classified as follows:

Hepato-bronchial fistulas,	2 cases
Gastro-biliary	1 case
Duodeno-biliary	36 cases
Biliary-colic	4 cases
(colon and gall bladder)	

Diagnosis is made by the presence of air or barium in the biliary tract. The formation of these fistulous connections usually depends upon the presence of a biliary calculus which has ulcerated through the gall bladder into the gastro-intestinal tract. Gastric and duodenal ulcers and carcinoma of the stomach are among the rarer causes. The only cases diagnosed by roentgen-ray visualizations are the four cases reported by Judd and Burden (Ann. Surg., 1925, 81, 305).³

BIBLIOGRAPHY⁴

1. ALBERTI, O.: Radiol. med., 1927, 14, 729.
2. ANZILOTTI, A.: Radiol. med., 1930, 17, 1039.
3. ARNTZEN, LEIF: Acta radiol., 1932, 13, 202.

³ From Year Book of Radiology, 1933.

⁴ This bibliography was taken from the 1933 Year Book of Radiology.

4. BEUTEL, A.: Röntgenpraxis, 1932, **4**, 326.
5. BIGNAMI, G., and AGATI, D.: Radiol. med., 1931, **18**, 545.
6. BUISSON, P.: Radiol. med., 1931, **18**, 689.
7. BUSI: Radiol. med., 1921, **8**, 122.
8. CANNANO, L., and COLA, G.: Radiol. med., 1931, **18**, 245.
9. COURVOISIER: See Radsiewsky, Ref. 41.
10. CRANE, A. W.: Am. Jour. Roentgenol. and Rad. Ther., 1931, **26**, 92.
11. DALSACE, JACQUES: Arch. d. mal. de l'app. digestif., 1930, **20**, 194.
12. DELHERM, DALSACE, THOYER-ROZAT, and CODET, P. P.: Pressé med., 1931, **39**, 302.
13. DIENST, CORNELIUS: Fortschr. a. d. Geb. d. Röntgenstrahlen, 1927, **36**, 674.
14. FISHBAUGH: See Kantor and Jaffin, Ref. 30.
15. FRAENKEL: Arch. f. klin. Chir., 1928, **153**, 407.
16. VON FRIEDRICH, L.: Fortschr. a. d. Geb. d. Röntgenstrahlen, 1929, **39**, 616.
17. FULLER, C. J.: Brit. Med. Jour., 1930, **1**, 279.
18. GATEWOOD and POPPENS, P. H.: Surg., Gynec. and Obst., 1922, **35**, 445.
19. GAVAZENNI, L., and LUSO, JONA A.: Riforma med., 1928, **44**, 1160.
20. GLASS and ISRAELSKI: Die Probe der retrograden Füllung der Gallenwege aus dem Duodenum mittels obturierender Duodenalsonde. Zentralbl. f. Radiol., 1932, **11**, 680.
21. GRABERGER, GOSTA: Acta radiol., 1931, **12**.
22. HABBE, J. E., and SMITH, L. A.: Jour. Am. Med. Assn., 1926, **86**, 476.
23. HAENISCH, F.: Acta radiol., 1926, **6**, 485.
24. HARDING, D. B.: Am. Jour. Roentgenol. and Rad. Ther., 1929, **22**, 36.
25. HAVLICEK, HANS: Fortscher., a. d. Geb. d. Röntgenstrahlen, 1925, **33**, 944.
26. HUNT and HERBST: Surg. Clin. North Am., **3**, 807.
27. HUTTER, K.: Arch. f. klin. Chir., 1927, **146**, 332.
28. JENKINSON, E. L., and BROUSE, I. E.: Am. Jour. Surg., 1931, **12**, 499.
29. JUDD, E. S., and BURDEN, V. G.: Four Cases of Biliary Colic Fistula. Ann. Surg., 1925, **81**, 305.
30. KANTOR, J. L., and JAFFIN, A. E.: RADIOLOGY, 1928, **10**, 10.
31. KEHR: Handbuch d. prakt. Chirurgie, **3**.
32. KERN: Fortschr. a. d. Geb. d. Röntgenstrahlen, 1931, **43**, 805.
33. KIRSCHNER and NORDMANN: Die Chirurgie, Berlin, 1927, **6**, 1.
34. KÖHLER: Grenzen des Normalen und Anfänge des Pathologischen im Röntgenbilde. Leipzig, 1928, p. 514.
35. KORTE: See Ref. 33.
36. LEWIN, E.: Röntgenpraxis, 1932, **4**, 222.
37. LONNERBLAD, LARS: Acta radiol., 1932, **13**, 551.
38. LUST: Fortschr. a. d. Geb. d. Röntgenstrahlen, 1931, **44**, 793.
39. MARTINOTTI: Minerva med., 1929, p. 335.
40. PREVOT: Röntgenpraxis, March, 1933, p. 177.
41. RADSIEWSKY: Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1902, **9**, 659.
42. REICH, LEO: Fortschr. a. d. Geb. d. Röntgenstrahlen, 1929, **40**, 698.
43. REIMANN: Fortschr. a. d. Geb. d. Röntgenstrahlen, 1930, **41**, 802.
44. ROBSON, A. W. M.: Brit. Med. Jour., 1909, **1**, 1050.
45. ROTH, SCHROENDER, and SCHLOTH: See Robson, Ref. 44.
46. SCHINZ, H. R., and others: Lehrbuch der Röntgendiagnostik, Leipzig, 1932.
47. SIGHINOLFI, P.: Bull. d. sc. med., 1926, **4**, 313.
48. STEPHENSON: See Kantor and Jaffin, Ref. 30.
49. WANGENSTEEN, O. H.: Ann. Surg., 1928, **87**, 54.
50. OHNELL, H., and LINDBLOM, K.: Acta radiol., 1929, **10**, 121.

ARTEFACTS IN ROENTGEN FILMS

By GEORGE C. HENNY, M.D., *Philadelphia*

Department of Roentgenology, Temple University School of Medicine

AN artefact in a roentgen film is a marking produced by an agent other than the x-ray through the part being radiographed. An artefact may be of any size or shape and may be either negative or positive in phase (may be exhibited as an area of film lighter than its surroundings—the negative phase—or darker than its surroundings—the positive phase).



Fig. 1. Film markings produced by excessive moisture and heat in the film storage room. In most places the emulsion is desensitized, but in one spot it is actually sensitized.

Every roentgenologist occasionally sees artefacts in his films: they appear even in the most carefully controlled laboratories. Sometimes the cause is easily traced but at other times it is very puzzling. The roentgenologist is apt first to think that the artefacts were produced in the manufacture of the films and may even change his brand of films on that account. However, experience has shown that artefacts produced in the manufacture of present-day films are rare. A review of the causes of artefacts in roentgen films will aid the roentgenologist to trace his difficulty in any particular case.

It must be kept in mind that the emulsion of the roentgen film is a very sensitive

substance, easily affected by light, stray x- or gamma rays, by mechanical manipulation, by gases and vapors (such as illuminating gas, hydrogen sulphide, ammonia, formalin vapor), and by other chemicals and by excessive moisture and heat (Fig. 1). The storage room for films should be free from all of these.

The most usual causes of artefacts are listed below.

I.—STRAY RADIATION

Variable marks on the film may be produced by stray radiation from a fluoroscope. In one instance, a fluoroscope twenty feet away from the radiographic room produced a series of parallel lines (multiple exposures of a metal bar as the fluoroscopic tube was moved) on the finished film. The fact that a fluoroscope can produce such marks is well recognized, but that it can do it at such distances may be overlooked. Any leakage from the x-ray therapy room must also be ruled out. This is best done by trial exposures, for even though the tube is "auto-protected," conditions may be such that stray radiation is reaching the radiographic or loading room.

If there are a number of radiographic rooms and a film is being carried from one of these to the dark room while an exposure is being made in another, stray radiation may strike the film being carried. Exposed and unexposed films must, of course, be adequately protected in the radiographic room. In one instance, nails which held down the lead covering of the cassette storage box had worked loose and came out. The lead was bent down somewhat, and when x-rays from the radiographic table fell on the box, there was enough leakage to produce an irregular blackening of the films with three black marks corresponding to the nail holes (Fig. 2). Radiation from radium or radon needles can produce marks on the films, but this is not apt to occur.

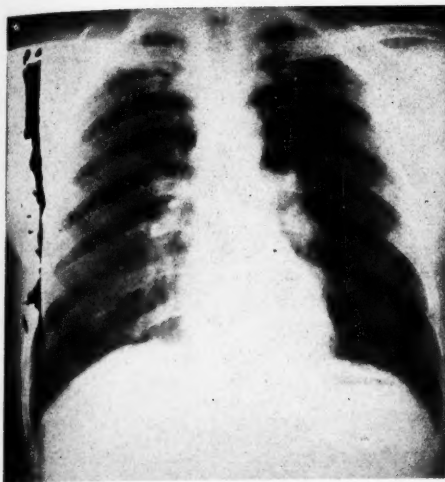


Fig. 2. Artefact caused by leakage of x-rays in cassette storage box where lead protection had become displaced. Only the 14 X 17 inch films were affected, as the others did not reach this height.

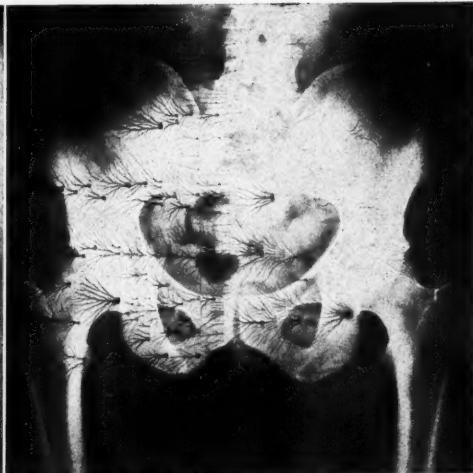


Fig. 3. Static marks produced by jerking the film out of a tightly packed box.

If a cassette is placed against a solid wall while a radiograph is being taken, there may be enough back-scattering to pass through the back of the cassette and thus show shadows of the supporting ribs.

Fog due to x-radiation or radium is approximately of equal density on both sides of the film. This can be tested by moistening a spot on each side of the film and scraping off the emulsion on that side. The densities of the two single coatings are then compared. If the fog is due to exposure to light, it is usually more pronounced on one side of the film than on the other.

If a package of films is accidentally exposed to x-rays the corrugations in the packing material will show up. On Eastman films, the shadow of the lead band placed in the box for this purpose becomes visible. Development of one of the films from the box without further exposure will reveal the fog.

II.—STATIC ELECTRICITY

When the relative humidity¹ is below

¹ "Relative humidity" is defined as the weight of water actually present per unit volume of air divided by the weight of water that is necessary to saturate that volume at the existing temperature.

about 20 per cent, it is very difficult to prevent static electrical discharges from leaving their marks on the film. The best way to prevent the generation of static electricity is to condition the air so that the relative humidity is at least 40 per cent. Where air conditioning equipment is not used this is impractical and it is necessary to avoid the generation and discharge of the electricity by other means.

Static electricity may be produced either in the body of the technician or locally in the film and cassette. The fact that walking on a carpet in a dry atmosphere will charge the body to a high potential (producing a small spark if a radiator or light switch is touched) is well known to almost everyone. The same thing can happen when walking on linoleum or cork floors. If the technician's body is highly charged and he touches a film, a spark will jump from his finger and make a mark on the film. The best way to prevent this is for the technician to touch a grounded metallic body before he touches the films in order to allow the charge to run off of his body. A convenient method is to have the bench, or at least the edge of the bench, covered with metal which is grounded.

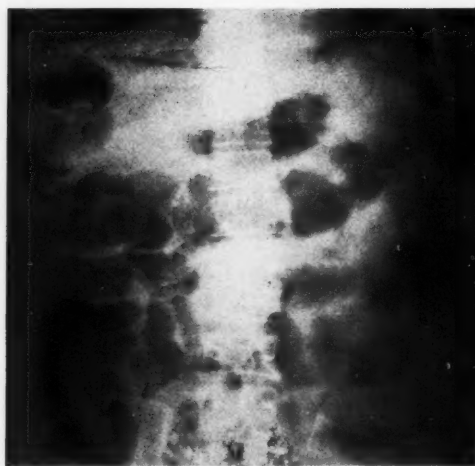


Fig. 4.

Fig. 4. A line of static marks produced by jerking the paper off the film.



Fig. 5.

Fig. 5. Static electricity marks resulting from handling the films with rubber gloves. By stroking the glove-covered finger across an undeveloped film a series of dots, as shown at the top of the illustration, could be produced. That conditions were favorable for the production of static electricity is shown by the presence of the typical branched markings at the bottom of the film.

Static electricity may be generated locally on the film or in the cassette in a number of ways. It is usually done by jerking the paper and film out of a full box; by jerking the film from the black paper and placing it quickly in the cassette; by shuffling the film in the cassette, and by opening the cassette quickly (after the exposure has been made) and touching it either with the fingers or to any electrically conducting body. The following are precautions (when air conditioning is not possible) to prevent the generation of static: Do not pack films from the old box in with six dozen in the new box; remove the film from the box, and the paper from the film slowly; do not shuffle the film to center it in the cassette; open the cassette slowly; touch a grounded metallic object before touching the films.

Static marks take one of three forms: (a) bush or tree-like markings—that is, branched; (b) small nearly round spots; (c) mottled or wool-like spots.

Jerking the film from the paper usually produces the typical tree-like markings: these are quite irregular, although they may appear in rows (Fig. 3) or lines (Fig.

4). Such markings may occur in the manufacture of the film, but it should be remembered that this is rare because the manufacturer is always on the lookout for them and operates under carefully controlled conditions of temperature and humidity. Markings produced in the manufacture of the film are apt to be regularly placed and in the same position on successive films, as along one edge, for instance.

When static marks are not of the typical tree-like variety they may be difficult to recognize. (Magnification of small spots frequently reveals their true nature.) If a film placed in a cassette is moved around with the fingers, static marks are liable to be produced. These marks will occur at the tip of each finger and may appear as a series of small black dots outlining the tip of the finger, with a branched marking at the center. Kodaloid covered intensifying screens are more apt to generate static electricity than others. Recently small black marks were appearing on some of our radiographs (Fig. 5), even in the central areas of the 14 × 17 inch films. Close examination of these suggested that they

might
appea
ordina
all or
preven
Invest
techni
gloves
solutio
handli
due to
artefac
produc
lightly
the m
condit
tion o
fact t
static
shown
moved
spots i
films w
rally,
at its
brough
In pic
film w
it is v
the la

Film
mecha
(Fig.
duced
it is
casset
at wil
face l
or sha
In ran
pointe
the si
has b
punct
coat,
before
The r
place
are us

might be due to static electricity, but their appearance was much different from the ordinary branched marks. Furthermore, all ordinary precautions were taken to prevent the production of static electricity. Investigation revealed that the dark room technician had started to wear rubber gloves to protect her hands from the solutions. She dried her fingers well before handling the films so the spots were not due to solution getting on the film. The artefacts which we were observing were produced when her gloved finger was lightly rubbed across the film: apparently the marks were of electrical origin. That conditions were favorable for the generation of static electricity was shown by the fact that there were typical branched static marks at the bottom of the film not shown in cut. When the gloves were removed, no more artefacts appeared. The spots in the central areas of the 14×17 inch films were at first misleading, because, naturally, one does not pick up such a film at its center. The films, however, were brought to the dark room in a film carrier. In picking up a 5×7 or an 8×10 inch film which is lying on a 14×17 inch film, it is very easy to touch the central area of the latter.

III.—MECHANICAL INJURY

Film emulsion is quite susceptible to mechanical injury. The crescent marks (Fig. 6) sometimes seen on films are produced by bending or crimping the film as it is slipped into or removed from the cassette. Such marks can be reproduced at will. If a film is slid over a rough surface before development, dark irregular or sharp black abrasion marks may result. In rare cases artefacts are produced by pointed objects (such as might occur on the side of an old developing tank which has become roughened). These points puncture the thin emulsion protective coat, allowing developer to enter here before it does to the rest of the emulsion. The result is that over-development takes place at these points. The darkened spots are usually not circular.

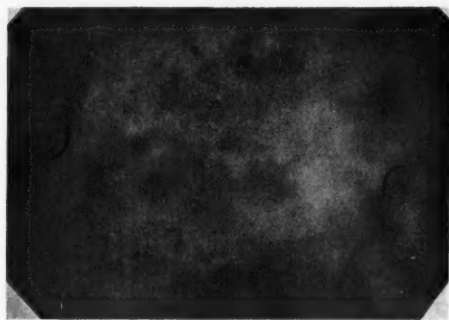


Fig. 6. Crescent-shaped markings result from crimping the film as it is picked up and slid into a cassette. The muddy marks at the top of the illustration were produced by touching the film with fingers wet with developer as it was being put into the hanger.

Melting of gelatin emulsion due to high temperature might also be placed under this heading. This is most frequently caused by holding the wet film against the illuminator. It might also be produced by hot water flowing through the washing compartment. Films are more easily injured from high temperature if they have been run through an exhausted fixing bath or one that was made without hardener. Reticulation—a puckered or net-like appearance of the film surfaces—results from excessive swelling of the gelatin in an uneven way and is brought about by sudden changes in temperature, such as removal of the film from a cool fixing bath to very warm wash water or *vice versa*.

IV.—CHEMICAL EFFECTS

(A) Marks produced by touching the undeveloped film with fingers contaminated with dark room solutions may be dark or light. If due to developer on the film, they will be dark (Fig. 6); if due to fixing solution, they will be light. Developer marks can usually be seen by reflected light on the surface of the finished film. Spattering the films with these solutions will have the same effect. Chemicals on the dark room bench may also get on the films.

(B) A film placed in a cassette that has recently been cleaned with hydrogen peroxide will be fogged.

(C) Another source of such artefacts is the use of a freshly made developing solution in which the salts have not yet been

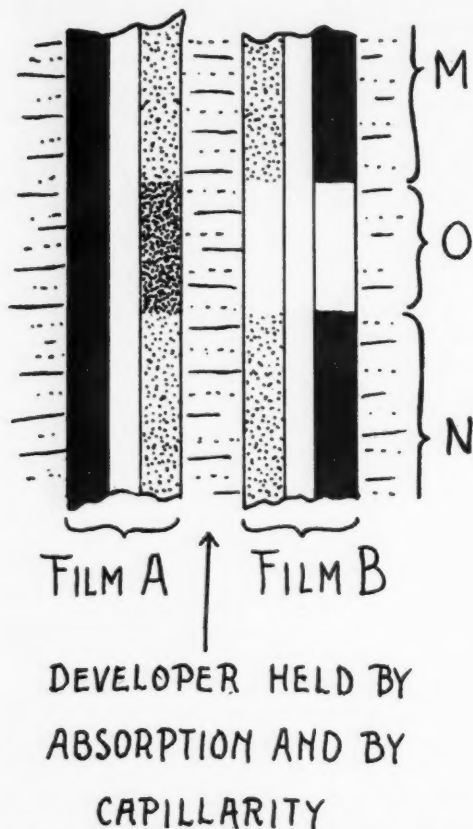


Fig. 7. Film A and Film B have come together in the developing solution but are separated by an extremely thin layer of developer. The outer layers of emulsion are strongly reduced (except at zone O of Film B which was protected from the x-rays), while the inner layers are incompletely reduced due to insufficiency of developer. This illustration was obtained from Robert R. Newell, M.D., of San Francisco.

dissolved. Round or comet-like spots may result from grains of salt settling on the film surface.

(D) The dark room technician may fail to notice that the developer does not cover the top edge of the film, in which case the finished film has a blank edge across the top.

(E) The negative image of one film may be transferred to another if the two are brought into contact after immersion in the developer, such contact as may

readily occur in a crowded tank or when a film becomes loose in its hanger. The mechanism by which this occurs is illustrated in Figure 7.² Film A and Film B have both been exposed to x-rays, but on Film B there was a protected area, O, which was not exposed. After immersion in the developer the films came in contact, leaving only a thin layer of developer between the adjacent surfaces. The outside layers of emulsion are strongly reduced, as shown, leaving a transparent spot at O on Film B where the shadow of the lead fell. Notice that the adjacent layers of the emulsion are incompletely reduced, due to insufficiency of developer. The action of the developer is divided evenly between the two emulsions, except at area O. Suppose that enough developer was caught between films to carry reduction 25 per cent to completion, as shown in zones M and N. At area O, none is used by the unexposed spot on Film B and all is thus available for Film A, which would, therefore, be 50 per cent reduced in that region.

(F) If the film comes in contact with the side of the tank, incomplete development of the emulsion over this area will result.

(G) Small air bubbles attaching themselves to the film as it is placed in the developer will result in under-developed spots at these points. Since only one side of the emulsion is affected, the marks are not very distinct. If the air bubbles attach themselves to the film after development has started, the marks will appear dark.

(H) It is good practice to use an acetic acid short stop bath between the development and fixing of the films because this neutralizes the basic reaction of the developer and thus protects the acid of the fixing bath. If the acetic acid is too strong (proper strength is 3.5 ounces of glacial acetic to a gallon of water), minute elevations on the emulsion will be produced

² I am indebted to Robert R. Newell, M.D., Professor of Medicine (Radiology), Stanford University Medical School, for this explanation of Figure 7, and for other suggestions in this paper.

Fig.
in suc
the le
but w
nosis

over i
appea
suffici
the a
solution
the fil
suffici
gas th
the ge
small
aggrav
(I)
oily, a
presen
coatim
chemi
absorb
If the
midity
shoul
in run
(J)
varyin
oxidat
the fil
is hel

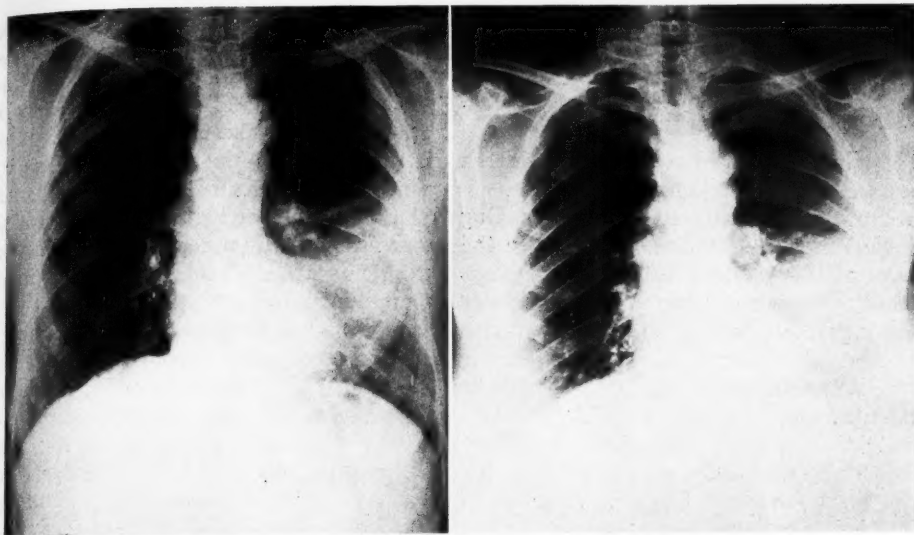


Fig. 8. The shadow of the heel of the anode of a line focus tube or of a long cone may be cast on the film in such a way as to be confusing. Figure 8-A (left) shows a routine radiograph of a patient with pathology in the left lung and with clear costophrenic sulci. Figure 8-B (right) shows the same patient at the same time, but with the shadow of a long cone falling on the lower portion of the film. In some cases an erroneous diagnosis of fluid in the costophrenic sulci might be made.

over its entire surface. Or, similarly, this appearance is produced if the film is not sufficiently washed before it is put into the acid fixing bath. The developing solution is alkaline and the transference of the film to the acid fixing bath without sufficient rinsing causes effervescence. The gas thus formed under the emulsion lifts the gelatin coating and produces numerous small blisters or bubbles. Warm solutions aggravate this condition.

(I) The surfaces of the film may appear oily, a condition which is caused by the presence of fixing solution in the gelatin coating, from insufficient washing. The chemicals retained are hygroscopic and absorb moisture from the atmosphere. If the film dries up due to a drop in humidity, a white deposit will be left. Films should be washed at least fifteen minutes in running water.

(J) General fogginess or streaks of varying density may be produced by oxidation of the developing solution on the film surface, incurred when the film is held out of the developing solution for

a prolonged time for inspection. High temperature of the dark room and insufficient sodium sulphite in the developing solution augment the condition.

(K) Fogginess or streaks may also be produced by developer which has become contaminated by mixing, or by using the solution in a metal (not enameled steel) container or by stirring it with a metal object. An enamelware or special compound tank should be used and the stirring paddle should be of wood.

(L) A dark streak, the length of the film, may be produced by contaminated solutions dripping off of the topmost clip in the film hanger.

(M) Streaks may be produced if an insufficiently rinsed film is placed in a fixing bath that has lost its acidity. In this case development continues in streaks, and one is apt to see a metallic lustre on the film surface (by reflected light), a result of silver deposit. Such deposits will not occur if the fixing bath is acid.

(N) Blue spots or stain may be incurred through the presence of iron in combination

with Farmer's reducer. These may be removed by immersing the film in a 5 per cent solution of potassium oxalate.

V.—OTHER CAUSES

Irregularly shaped transparent marks may be produced by barium sulphate on the front side of cassettes, on the covering of the Potter-Bucky diaphragm, or in the grain of the veneer table top through which the exposures are made. Irregular markings may also be produced by wrinkles in the skin, warts, fibromas, adhesive tape, iodoform and other opaque powders or ointments. Braids of hair may cast a shadow. Even a thin silk night-dress may show on the film because it is weighted with tin or barium, whereas a thick cotton cloth is less apt to show. A nurse's fingers may cast very disturbing shadows. Artefacts arising from dirt, bits of paper or injuries on the double intensifying screens are very frequent, and can be recognized by the extreme sharpness of their edges. It is possible for bits of metal (a flake of nickel plating from the spring of the cassette, for example) to get behind the front screen. A shadow will be cast on the film and yet the bit of metal not be visible to the eye.

A portion of a radiograph may be blurred while the rest of it is sharply defined, due to poor contact between the intensifying screens and film. Contact may be tested by placing a fine wire mesh immediately on top of the cassette and then exposing to x-rays from a tube about forty inches away. After the film has been processed, poor contact is easily detected by fuzziness of some of the wire shadows. Incidentally, a good idea of the resolving power of the screens may be obtained from this same film.

The parallel lines of the Potter-Bucky diaphragm grid are easily recognized. If the tube is off the Potter-Bucky diaphragm center, a cutting down of x-ray intensity or even complete blocking occurs on the portion of the film which is farthest off center. In certain line focus tubes, the angle be-

tween the central ray and the target face is sufficiently narrow to permit the production of an important artefact. The shadow of the "heel" of the anode may be projected on a chest film in such a place as to permit of the possibility of an erroneous diagnosis of fluid in the costophrenic sulci. In Figure 8 such a shadow was produced by a cone. A dark spot on a film may be produced by a hole in an aluminum filter.

Fog may be produced by faulty intensifying screens which have a very large lag. To test this, cover one-half of a film on both sides with black paper and place it for twenty-four hours in a cassette which has recently been exposed to x-rays. Develop the film without exposure and if the uncovered portion of the film shows fog, the screens are at fault. Fog may also be produced by accidental exposure to light, by extraneous light entering the dark room, or by prolonged exposure to the safelight. Safelights are designed for bulbs of a given candle power, and are "safe" for a definitely limited exposure. If a higher candle power bulb is inserted, due allowance must be made for the increased tendency to fog.

Irregular markings on films, usually are noticeable by reflected light, are produced by scum on the solutions. Where organic matter is present in the water used in mixing the solutions, scum is likely to form. It should be removed from the solutions the first thing in the morning by skimming with strips of blotting paper.

Deterioration of x-ray film from moisture usually produces a granular appearance, which may show up as parallel lines found to correspond to the corrugations of the film box packing. Sometimes evidence of the moisture can be seen on the outside of the film box.

I wish to express my appreciation for the assistance given me by Mr. Charles W. Smith, representative of the Eastman Kodak Company, and to Mr. R. K. Perrine, of the du Pont Film Company, for two of the illustrations.

ONE THOUSAND SPENOIDS EXAMINED IN BOTH THE GRANGER AND MENTO-VERTEX POSITIONS¹

By AMÉDÉE GRANGER, M.D., *New Orleans*

ALREADY, in 1932, we had summarized briefly a comparative study² of about forty sphenoids, examined in both the Granger and mento-vertex positions. Since then we have ex-

were radiographed in both the Granger and mento-vertex positions.

This intensive study convinced us more than ever of the diagnostic value of the Granger line and we do not fear contradic-



Fig. 1-A. Small amount of pus in the right sphenoid, diagnosed by the obliteration of the mesial portion of the right half of the Granger line. Radiograph made in the Granger position.



Fig. 1-B. Small amount of pus in the right sphenoid which could not be differentiated from a mild degree of hyperplasia, capable of causing the slight increase in density of the right sphenoid. Radiograph made in the mento-vertex position of the same case as in Figure 1-A.

amined over a thousand sphenoids, 633 from March 15 to June 15, 1933, and 394 from May 1 to August 1, 1934, all of which

tion when we state that by a careful study of that line alone a correct roentgen diagnosis of the condition of the sphenoid sinuses can be made in at least 95 per cent of the cases examined.

As previously stated in our monograph, this study, which confirmed our experimental work with the filled skulls, has

¹Presented as a clinic before the Radiological Society of North America, at the Twentieth Annual Meeting, in Memphis, Tenn., Dec. 3-7, 1934.

²Radiological Study of the Paranasal Sinuses and Mastoids. Lea & Febiger.

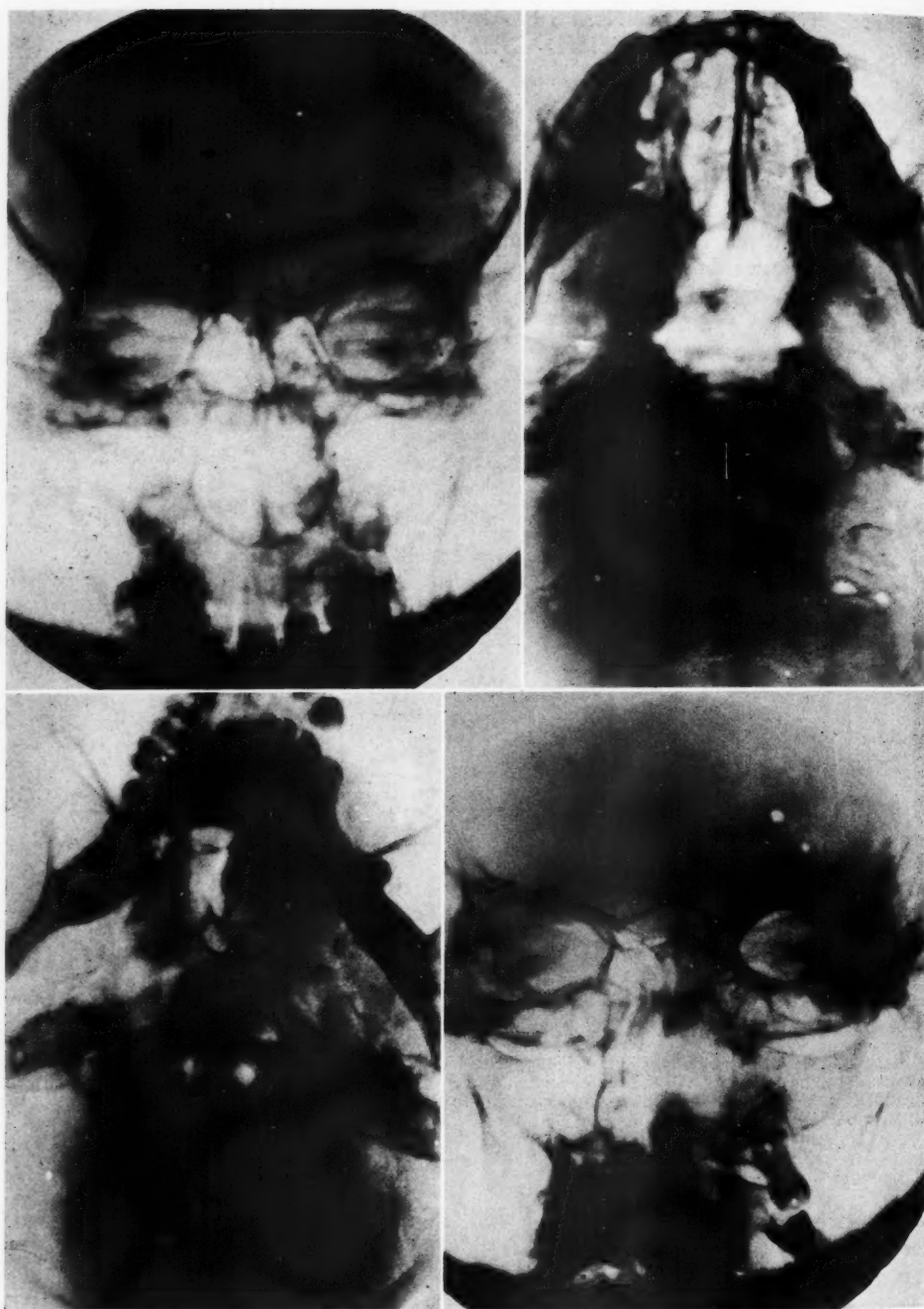


Fig. 2-A (*upper left*). Hyperplastic sphenoiditis on the right side. Diagnosed by the rarefaction, broadening, and indistinct lower edge of the right half of the Granger line. Radiograph made in the Granger position.

Fig. 2-B (*upper right*). Right-sided hyperplastic sphenoiditis, which cannot be diagnosed because both sphenoids are clear. Radiograph made in the mento-vertex position of the same case as in Figure 2-A.

Fig. 3-A (*lower left*). Cancer of the right naris. The marked opacity of the right sphenoid would certainly indicate gross pathology of that sinus. Radiograph made in the mento-vertex position.

Fig. 3-B (*lower right*). Cancer of the right naris. The clear and distinct Granger line rules out any pathology in the sphenoid sinuses. Radiograph made in the Granger position of the same case as in Figure 3-A.

proven to us that radiographs made in the mento-vertex position, first, do not have positive and readily identified boundary landmarks for the sphenoid and ethmoid, and second, that perfect duplicate radiographs of the same head are rarely obtainable. The position is more uncomfortable and, if the neck is short and—what is not uncommon in cases of arthritis—if the neck is stiff, it is extremely difficult and even at times impossible to make satisfactory radiographs in the mento-vertex position.

The superiority of the Granger position was even more manifest when the radiographs were studied for signs of healthy and diseased conditions of the sphenoids.

In the mento-vertex radiographs, the sphenoids show either clear or more or less opaque. A very slight degree of opacity such as might be caused by a small amount of pus in one sphenoid or by a slight or moderate degree of hyperplasia of its lining membrane can be detected only if the other sphenoid appears clear, and even then it is impossible to say which of these two pathologic processes is causing the slight opacity. We need not insist upon the value of this information to the otolaryngologist.

We have been able to recognize a small amount of pus in the Granger radiograph (Fig. 1-A) because of the obliteration of part of the Granger line by the pus flowing against it in a correctly made radiograph, which could not have been diagnosed in the mento-vertex radiograph (Fig. 1-B).

This diagnosis was confirmed in some cases by the appearance of the Granger line after therapeutic drainage, with relief of the clinical symptoms, and in other cases by the appearance of the Granger line in

radiographs made with a faulty technic, *i.e.*, by tilting the tube instead of the head of the patient to the required angle, in which case the pus flows against the anterior wall of the sphenoid and not against the anterior portion of its roof, *i.e.*, the Granger line (Figs. 15 and 16 in the author's "Paranasal Sinuses and Mastoids").

We have also repeatedly made the diagnosis of hyperplastic sphenoiditis (Fig. 2-A) when the Granger line was either broadened, rarefied, indistinct, or shaded along its lower edge. This condition could not be diagnosed in the mento-vertex radiograph (Fig. 2-B).

Of course extensive pathology such as large quantities of pus, extensive hyperplasia, or granular or polypoid changes, with or without pus, cause opacity of the diseased sphenoid in both radiographs, but in addition the Granger line is always obliterated on the diseased side in our radiographs: we must remind you that a clear and distinct Granger line with sharp edges means a healthy sphenoid.

We have seen not a few opaque sphenoids in mento-vertex radiographs (Fig. 3-A) which were not caused by disease of those sinuses but by marked occlusion of the naris from carcinoma (Fig. 3-A), from extensive polyposis, and even from greatly hypertrophied turbinates, when the presence of a clear or even a fairly distinct Granger line in radiographs made in our position (Fig. 3-B) positively and correctly ruled out any pathology of the sphenoid other than a slight or moderate amount of hyperplasia of its mucosa. This was later confirmed at operation or after painstaking rhinological investigation.

SOME REFLECTIONS ON THE ETIOLOGY OF KÖHLER'S DISEASE

By DR. A. ZEITLIN, *Moscow, U. S. S. R.*
State Institute of Radiology

Translated from the French by E. T. LEDDY, M.D.

THE localization of the lesions in Köhler's disease differs from those of other osseous affections of a juvenile osteochondropathic type in that the whole metatarsal head which is involved may be removed surgically without greatly interfering with the function of the foot. This operation, carried out for therapeutic reasons, has allowed us the opportunity to study in several cases the pathologic anatomy of the changes in the bone. Nevertheless, a very detailed study of the histologic picture has given us no clew to the underlying cause of this disease. Concerning this point there is in the literature nothing but hypotheses, more or less solidly established, based on the opinions of the various authors.

The microscopic changes in the metatarsal head in the earliest stages of the disease of Köhler II present the histologic picture of an aseptic necrosis of bone, followed by fracture; differences of opinion begin when the attempt is made to explain this necrosis. Some hold that it is the result of a repeated traumatism (Kappis, Freiberg, and Speed); others, that it results from a micotic embolism of the small vessels (Axhausen); a third group claims that it results from an endarteritis of the vessels of the periosteum and of the capsule (König and Rauch, Rösner and Weil, Holst and Chandrikoff); a fourth group states that the process is a fibrous osteitis, a tuberculosis, an osteomyelitis, etc. It should be mentioned that several authors are of the opinion that a local cause is not sufficient to explain the changes in the involved bone, so they add supplementary factors to the local status of the bone, such as some special constitutional predisposition (Liek and Altschul), or some endocrine disturbance (Bragard and Frommé), or finally the inanition or exhaustion of the body's reserve following

some severe disease (Alberti, Holst and Chandrikoff, and Kienböck). However, in reviewing the histories of patients with Köhler's disease we find that in the majority of instances there was no confirmation of these theories. G. Reinberg was quite certainly correct when he wrote, in 1926, that all discussion of the bodily constitution and of the internal secretions in Köhler's disease be stopped, for such are nothing but the prevailing fashions in medicine. Here one might make the exception of a "gracious" constitution with fragile bones and weakened muscles. In this case the diminution of mechanical resistance and an increased vulnerability of the tissues would favor the development of a local process in the metatarsus, statistical evidence showing that this affection is most common in adolescence and in the female sex. It is possible also that a general debility of the body which has been noted in some cases would have the same effect. However, the possibility of modifying this constitutional factor, that of age and sex, is proven by the fact, noted by G. Reinberg and confirmed by us, that Köhler's disease does not occur in dancers and young girls who have been trained in institutes of physical culture, a fact which is explained by the systematic exercise of the legs and the harmonious development of the muscles.

All of these considerations lead to the conclusion that it seems more logical and plausible to look for some local process as the cause for Köhler's disease which is a local lesion, as, for example, the functional laxity or the insufficiency of the osteo-muscular mechanism of the foot. The importance of the static and mechanical condition of the body in the development of Köhler's disease has drawn the attention of investigators for a considerable length of time. Among these

conditions we do not take seriously the height of the heel of women's shoes, which has been the subject of much attention in the literature as a cause of this disease, for the fact remains that millions of women wear high-heeled shoes while the incidence of Köhler's disease is extremely low. According to the author's way of thinking, the structural and anatomic peculiarities and variations in the make-up of the foot are of much more importance. Almost all authors, regardless of how they regard the nature of this affection, assign a certain importance to the overloading ("surcharge") of the anterior portion of the foot; in fact, some authors state that this overloading is the main factor in the etiology of the lesion. Engelman, Baensch, Lang, Düring, Sonntag, and others have pointed out the importance of flat foot in causing Köhler's disease. Momburg is of the opinion that, in walking, at the moment the heel is lifted the principal overload falls on the second metatarsal, which is the commonest site of the lesion. Holst, Chandrikoff, and others state that at the moment the heel is lifted the imprint of the anterior portion of the sole is deepest in the region of the head of the second metatarsal.

Our attention was called to the question of the etiology of Köhler's disease, during a radiologic study of the changes in the foot in Deutschländer's disease, *pied forcé*, or march foot, according to the terminology of various authors. Our attention was drawn by the fact that these two changes frequently appear in the foot of the same subject. We have six such cases in our personal records, and we have encountered three others in the literature among the radiographs of patients with Deutschländer's disease. Of great interest are the publications of Axhausen and Schnee who have observed both conditions in the same metatarsal bone. One naturally thinks, therefore, that there is some relationship or a parallelism in the two affections, an idea that was advanced by Bragard and Schnee. In our opinion this relationship is due to the identity of

the causes which favor the development of the lesion in one or the other portion of the metatarsus.

Like the majority of English and French authors, we do not think that Deutschländer's disease is a separate nosologic unit. The condition which we have been recently calling a separate disease entity is none other than a lesion first described, in 1855, by Breithaupt, and known in different countries by different names, such as syndesmitis metatars., osteoperiostitis metatars., march foot, Marschfraktur, *pied forcé*, etc. The most important characteristic of this affection is the overloading of the foot (*pied forcé*, of the French authors). The acute or subacute development of this disease is generally preceded by some anatomic changes which indicate the structural and functional weakness of the bones of the foot; these changes may be detected in the radiograph. A. Morton has given us the following outline of these changes: (1) shortening of the first metatarsal, (2) backward displacement of the sesamoids, (3) enlargement of the space between the first and second cuneiforms, (4) thickening of the medial border of the first metatarsal, (5) thickening of the diaphysis of the second metatarsal. We have found these signs of Morton in different combinations in the greater part of 18 radiographs of *pied forcé* which we have had the opportunity of studying. In reviewing the radiographs of patients with Köhler's disease we have found these same signs of Morton in a considerable number of cases. In 22 radiographs of patients with Köhler's disease which we have studied we found shortening of the first metatarsal three times, displacement of the sesamoids 14 times, enlargement of the space between the cuneiforms 16 times, thickening of the border of the first metatarsal 16 times, and thickening of the third and fourth metatarsal 19 times. In three radiographs these signs were not definite and in only three instances were they completely absent.

These findings lead us to suppose that

in the etiology of Köhler's and Deutschländer's diseases the weakening of the foot or its overloading play a very important rôle. The difference in localization of the two conditions may be explained to a certain extent by the age of the patient. An alteration in the head of the metatarsal is due to the fact that it develops earlier here than in the diaphysis. In our own cases, and in those we have cited from the literature in which we had a combination of the two conditions and in which we found changes in the diaphysis, the important changes in the head of the metatarsal were already present. One might suppose that the head of the metatarsal, rich in spongy tissue and covered by a thin cortical layer, would be the first to suffer, and it is only with advancing age when it has become more resistant that the changes involve the diaphysis. It is just at this period when an increase in body weight exerts greater stress on the metatarsus.

The pathologic anatomy of the process in the head of the metatarsal in the disease of Köhler II may be explained other than that it is a necrosis due to obliteration of vessels. In a study by the aid of the spectroradiograph of the fine structure of bone both normal and "overloaded," Henschen found changes in the latter similar to those which are found on analysis of "stressed" metal. There are changes in the groupings of the crystalline system at the point where the pressure is greatest, and also the formation of a line or a zone of slipping along which finally there are formed fine fissures and gaps. This process is the forerunner of the formation of microscopic and macroscopic fractures, and the destruction of the trabeculae of the bone. Finally these changes take on the appearance of compression fractures of the spongy tissue resulting from a long-continued pressure. The process may be compared to that which is observed in the spondylitis of Rummel-Verneuil in which the settling of the body of the vertebrae does not occur until a long time after the trauma.

Köhler's disease is often compared with Legg-Calvé-Perthes' disease, but we feel that the analogy to Kienböck's disease of the semilunar bone is closer. In both these affections the process takes place in a bone already formed, possessing a spongy structure and a thin cortical, whereas in Legg-Calvé-Perthes' disease we have an infantile epiphysis of the femur in the process of growth, rich in cartilage and in the elements of new-formed bone. Therefore, the successions of osseous changes noted radiologically in the head of the metatarsal (Köhler's disease) and in the lunate bone (Kienböck's disease) are completely analogous. The same is true of the osseous deformities in the two affections, while the possibility of a complete restoration to normal is a characteristic of Perthes' disease. The etiobiologic factors in the two conditions seem to be identical and the rôle of micro-traumatism in Kienböck's disease has been emphasized by that author on many occasions.

Because of the insignificant rôle which the cartilage plays in the pathologic changes in the two affections, might it not be more correct to speak not of osteochondropathy but of osteopathy (micro-traumatic osteopathy)? By the theory of weak foot, and the overloading of the foot in Köhler's disease the fact that the changes are most frequent in the second metatarsal is easily explained, even though they may also occur in the head of the third or fourth metatarsal. In the radiograph of the foot the prominence of the second metatarsal in comparison with the others can be easily seen in the majority of cases. G. Reinberg admits the rôle of walking or rather the position of the axis of flexion of the foot in regard to the direction of movement. Morton develops in a more detailed way the study of weak foot and of the overloading of the foot. According to him, in walking or in standing the heads of all the metatarsals touch the ground equally, but the load which each one of them carries depends on the division of weight, which, in turn, depends on the particular make-up of the foot in question.

In weak foot and in exaggerated pronation the center of gravity of the body is shifted from its normal position between the first and second metatarsals, more externally and corresponds to the position of the third or fourth metatarsal more than to that of the second. The metatarsal most traumatized thereby is, therefore, the one most affected.

The question of the thickening of the metatarsal diaphysis in Köhler's disease is rarely discussed; the fact is simply stated without being explained. As we have just stated, Morton includes thickening of the diaphysis of the second metatarsal among the symptoms of weak foot, and sees the cause of this fact in a compensatory hyperostosis as a result of a chronic overloading of the involved foot. Accordingly, the change in the heads of the third and fourth metatarsals produces the thickening of the corresponding diaphysis, that is to say, the one which has the greatest stress.

We have pointed out elsewhere the probable rôle of the interosseous muscles in the development of this hyperostosis. According to Jansen, these muscles which are inserted along the whole of the metatarsal diaphysis take a very important part in the act of walking by fixing the metatarsals to the phalanges, and *vice versa*. When static conditions are changed this reciprocal relationship is changed also, in the sense that there is an increase of work thrown onto those interosseous muscles which are inserted into the most affected metatarsal. The permanent tension placed on the periosteum leads to its hyperplasia and thickening, with a resulting reconstruction of the bone in the involved zone.

According to Hackenbroch, one observes frequently a thickening of a metatarsal which is congenitally short, or one which has been shortened operatively. The author explains this fact as due to an excessive overload.

Our radiographs of Köhler's disease have come to us from different institutes, a fact which has hindered us from getting an exact clinical history of the age at which the lesion started and the way in which it developed. Nor have we been able to clear up the questions about the thickening of the metatarsal, whether it occurs simultaneously with the changes in the head, or after them. We have radiographs in which the changes in the metatarsal are relatively recent (stages 1 and 2), in which the hyperostosis is well pronounced, and others of analogous cases with very little thickening of the diaphysis, or even none at all. In the more advanced stages (3 and 4) the hyperostosis is present in most cases.

Therefore in Köhler's disease an anatomical or structural weakness of the musculature of the foot, with an exaggerated overloading of one of the metatarsals, is one of the important causes of the changes which take place in the head of that metatarsal. Fracture is the result of overloading of the bone which results from molecular changes in the fine structure of the bone, with subsequent gross changes. In young subjects it is the head of the metatarsal (Köhler's disease) which is most involved, while at a more advanced age the involvement is in the diaphysis (Deutschländer's disease). The two processes are accompanied by thickening of the diaphysis.

EDITORIAL

LEON J. MENVILLE, M.D., *Editor*

HOWARD P. DOUB, M.D., *Associate Editor*

COUTARD'S METHOD OF TREATING CANCER BY IRRADIATION THERAPY

Coutard, of Paris, in 1920 began the treatment of cancer by irradiation therapy, using a technic of his own, based on principles obtained by certain experimenters. In one instance it was observed experimentally that a dose of x-rays large enough to sterilize a rabbit's testicle produced a necrosis of the skin when given in a single dose. However, when given in five equal doses, administered at intervals over a period of from thirteen to seventeen days, it produced sterilization but without destruction of the skin. In other words, while the effect on the embryonic cells was about the same the skin was not damaged.

Coutard reports that between the years of 1920 and 1926 he treated about 216 cases of throat malignancies, most of which were inoperable, with the result that 20 per cent of the cases treated were symptom-free at the end of five years.

These excellent results of Coutard's treatment have been the cause of numberless radiologists using his method in the treatment of cancer of the throat. In many instances, however, certain modifications of his technic were deemed advisable, principally because his method of treatment is a prolonged and expensive procedure and for this reason can be applied in but a few of the large medical institutions. However, the reports from the various modifications of his method are most gratifying.

Coutard's method of irradiation is now being applied in malignancies other than those of the throat, and the results are apparently the same.

The intense interest manifested in this form of treating cancer has been the occasion of calling together some of the outstanding radiologists of the country in a discussion of this subject at the Fiftieth Anniversary of the Memorial Hospital, New York City. We append hereto the result of this conference which is most edifying and instructive.

A SYMPOSIUM ON THE TREATMENT OF PHARYNGEAL CANCER BY THE DIVIDED OR PROTRACTED DOSE PRINCIPLE OF EXTERNAL RADIATION

Edited by HAYES E. MARTIN, M.D., *and* MAURICE LENZ, M.D., *New York City*

On May 25, 1934, as a part of the program at the Fiftieth Anniversary Celebration of the founding of the Memorial Hospital, New York City, a symposium was held on the divided or protracted dose principle of external radiation in the treatment of pharyngeal cancer. There were present, as active participants in this symposium, the following: W. Edward Chamberlain, M.D., Temple University Hospital, Philadelphia; Edwin C. Ernst, M.D., St. Louis; G. Failla, D.Sc., Memorial Hospital, New York City; Maurice Lenz, M.D., Presbyterian and Montefiore Hospitals, New York City; Hayes E. Martin, M.D., Memorial Hospital, New York City; Walter L. Mattick, M.D., State Institute for the Study of Malignant Disease, Buffalo; Edwin A. Merritt, M.D., Warwick Cancer Clinic, Garfield Memorial

Hospital, Washington, D. C., and Bernard P. Widmann, M.D., Philadelphia General Hospital, Philadelphia.

Each of the above-mentioned investigators gave a ten-minute description of his technic, after which the following treatment factors were discussed separately, and in turn:

1. Sources of radiation:
 - (a) X-rays
 - (b) Radium element packs.
2. Physical factors of x-rays and radium packs:
 - (a) Kilovoltage
 - (b) Milliampereage
 - (c) Radium content
 - (d) Target-skin distance or radium-skin distance
 - (e) Filter.

3. Total treatment period in days.
4. Interval of treatments (daily, twice daily, every other day, etc.).
5. Size of individual dose or daily dose in roentgens.
6. Size, number, position, and shape of skin portals.
7. Total dose in roentgens.
8. Reactions in the skin and mucosa.
9. Anatomic varieties of cancer treated.
10. Histologic varieties of cancer treated.
11. Combination of interstitial radon with divided doses of external radiation.

It was hoped, thereby, to secure a cross-section of the American opinion on the divided dose or protracted dose method of external radiation as it existed in 1934.

In order to present the various technics, and the opinions expressed during the discussion in the most compact and available manner, the material has been condensed and edited with the hope that the reader might, thereby, be spared a great deal of time and effort in obtaining exact information as to this symposium's discussions and opinions.

1. *Sources of Radiation.*—All observers had used mainly x-rays in the neighborhood of 200 K.V. Martin reported the use of 700 K.V. x-rays in a few cases. Martin, Mattick, and Widmann also reported the use of radium element packs in a limited number of cases.

2. *Physical Factors of X-rays and Radium Packs* (a) *Kilovoltage.*—Most of the x-rays used were in the neighborhood of 200 K.V., the variation being from 160 K.V., constant potential (Chamberlain), to 220 K.V. peak (Merritt). The apparent reason for the choice in this regard was that in all clinics the highest voltage available was used. Ernst recommended that in reporting voltage, one should refer to the effective voltage, rather than kilovolts peak. Chamberlain stated that physical measurements indicate that a constant potential source at 160 K.V. produces an x-ray beam having a shorter effective wave length than 200 K.V. peak from a pulsating generator. At the Memorial Hospital, the 700 K.V. machine, though highly desirable in this method of treatment, can take care of only a small percentage of the cases requiring treatment.

The radium packs used at the Memorial Hospital, New York City, and the Buffalo State Institute contain four grams, and that used at the Philadelphia General Hospital, two

grams of radium. The relatively long time required for individual treatments by these radium packs makes it impossible to care for more than a small percentage of the cases requiring treatment by the divided dose method in any of these clinics.

(b) *Milliamperage.*—Practically all observers had originally used 200 K.V. x-rays at 4 to 5 milliamperes. Lenz had originally used both 4 and 8 milliamperes. Lenz, Martin, Mattick, Merritt, and Widmann had subsequently also employed from 20 to 30 milliamperes, which they preferred because the higher milliamperage permitted a shorter treatment time (8 to 10 minutes, as against 40 to 80 minutes) in the individual treatments. With a limited number of treatment units of the higher intensities, four to five times as many cases can be treated, and the patients can be spared the fatigue and discomfort of such comparatively long exposures.

Of those who had used both amperages, all except Lenz were of the opinion that there was little, if any, difference in the physiologic effect between the two, with equal doses expressed in roentgens. Lenz believed that there was better ultimate recovery of the skin and subcutaneous tissues with the use of the lower intensities, especially in the use of large fields. Chamberlain had used only 5 milliamperes, and was unwilling to increase his current factor because of Coutard's insistence upon the paramount importance of a low r-afflux in this type of work. Gendreau, in the general discussion, stressed this point. Failla suggested that the difference in intensity and treatment time as between 4 and 30 milliamperes was hardly sufficient to account for a different physiologic effect.

(c) *Target-skin Distance or Radium-skin Distance.*—In no cases had distances less than 50 centimeters been used with x-radiation. Chamberlain, Ernst, Lenz, Martin, and Mattick had used distances up to 80 centimeters. It was agreed that distances greater than 60 to 80 centimeters are neither necessary nor economically sound.

In the use of radium element packs, both 6 and 10 cm. radium-skin distances had been employed. Widmann had used a distance of 4 cm. in a few cases. Martin stated that distances greater than 10 cm. would undoubtedly be advantageous, but since a radium pack dose, equivalent *physiologically* to about 350 to 400 r with 200 K.V. x-rays would require at least

two hours (8,000 mg.-hr.) with a 4-gram element pack at 10 cm., it is readily understood why great distances are impractical, when daily treatments of such lengths must be given over a period of from 20 to 30 days or longer.¹

(d) *Filter*.—There was some difference of opinion as to the best thickness of filter. Most of those present had used a filter of 2 mm. of Cu (or its equivalent) plus a secondary filter of 1 to 2 mm. of Al (Chamberlain, Ernst, Lenz, Merritt, and Widmann). This thickness of filter was used because of the conviction that the quality of the beam was thereby rendered harder and (with equal depth doses) less damaging to the skin than less heavily filtered x-radiation.

Martin and Mattick had used filters of 0.5 mm. Cu + 1 to 2 mm. of Al on the basis of Failla's investigations. Failla stated that his physical investigations indicated that the quality of a beam of x-rays produced at 200 K.V. is not materially improved by the use of a greater filter than 0.5 mm. of Cu, although the quantity is, of course, reduced by greater filters. It was his opinion that the use of 2 mm. of Cu filter with 200 K.V. x-rays is, therefore, wasteful from the economic standpoint. Those using heavier filters were of the opinion that Failla's physical conclusions were not borne out by clinical observations.

Mattick and Merritt had used Thoraes filters in a few cases, on account of their theoretical advantages. Martin reported that with 700 K.V. x-rays, Failla had recommended a filter of 5 mm. of Cu on economic grounds, which had thereafter been used in all treatments by this unit. With the radium element packs, a filter of from 2 to 3 mm. of brass or its equivalent had been used in all cases.

3. *Total Treatment Period in Days*.—The consensus of opinion was that a treatment period of from 20 to 30 days was best in the average case of pharyngeal cancer. Lenz preferred a treatment period of 30 days or longer in all cases. Martin had formerly used shorter treatment periods of from 10 to 14 days, which he had discontinued in favor of a longer, 20- to 30-day period (excluding Sundays), extending it to 40 to 50 days in certain radioresistant growths outside the pharynx.

¹ Using the inverse square law as a rough basis for calculating dosage, a dose of 8,000 mg.-hr. at 10 cm., given in two hours, would correspond to 18,000 mg.-hr. at 15 cm., and a treatment time of four and one-half hours. A daily treatment of such length would hardly be practical.

Merritt employed a treatment period of 20 days (excluding Sundays) in most cases, but in a few instances had extended treatment over about 50 days. Chamberlain also reported the use of 50- to 60-day periods in a few cases. It was the majority opinion that unusually long periods (over 30 days) are not advantageous in the average case of pharyngeal cancer. In some cases, Widmann had used two 10-day treatment periods separated by a rest interval of two weeks.

4. *Interval of Treatments (Daily, Twice Daily, Every Other Day, Etc.)*.—As a general rule, all speakers preferred to give one treatment per day to alternate skin portals on either side of the pharynx. In the case of more than two portals cross-firing on the same lesion, the portals were irradiated, one per day, in rotation. There was no report of the administration of two treatments daily with an interval of several hours' rest between treatments, as recommended originally by Coutard. Chamberlain preferred daily treatments, including Sundays and holidays, and insisted upon each portal receiving a daily dose. He stated that the administration of 300 r to right and left portals on alternate days was distinctly less rational than the daily administration of 150 r to each side. Martin reported giving treatment to two portals daily in the case of widely separated lesions, such as to the nasopharynx and a cervical metastasis, in which cases, one portal each to the cheek and one to the neck would be treated each day. There was no report of deliberately interrupting the sequence of treatments for several days before completing the series, except by Widmann, who had more recently changed his technic to an uninterrupted series.

5. *Size of Individual Dose or Daily Dose in Roentgens*.—The size of the daily dose depended to some extent on the size of the skin portal. All dosages mentioned below are expressed in roentgens measured at the longest target-skin distance, and in air without back-scattering.

Chamberlain, using fields of from 50 to 300 sq. cm., treated right and left portals daily, 110 r to each. In a general way, such a daily dose of 110 r to each side may be compared with a dose of 220 r, administered to alternate sides on alternate days. He based his insistence concerning the smaller daily dose to each portal, upon his belief that there is more skin recovery during the first twenty-four hours than during the second.

Ernst also treated two portals daily, giving 200 r to an 8 × 10 cm. portal to the side of the lesion, and 100 r to a portal of the same size on the side opposite the lesion. After 20 days, in some cases, he gave 20 daily treatments of 100 r each to a posterior portal.

Lenz varied the dose, depending on the necessary size of the skin portal. With portals varying from 6 × 8 cm. to 10 × 10 cm., he gave from 300 to 400 r daily. He had used 500 r daily with fields of 6 × 8 cm., but had discontinued such dosage, and advised against it. Lenz and Martin both advised a moderate variation of the daily dose with average portals, depending on the tolerance of the patient and the reaction of the primary lesion.

Martin, using smaller circular portals, 7 to 8 cm., whenever possible, gave an average daily dose of 350 r. This daily dose may vary from 300 to 400 r with portals varying from 6 cm. to 10 cm. in diameter. With the 700 K.V. x-rays, larger daily doses of 400 to 450 r were tolerated with about the same physiologic effect as the above-mentioned doses at 200 K.V. Mattick, using large fields in mostly all cases (10 × 15 cm.), gave daily doses to alternate portals of 320 r. Merritt had used daily doses of from 200 to 300 r, depending on the size of the field, 8 × 10 cm. to 10 × 15 cm. Widmann had used a daily dose of 300 r, irrespective of the size of the field (10 × 10 to 10 × 20 cm.).

6. Size, Number, Position, and Shape of Skin Portals.—The size of the skin portals varied from 6 × 6 cm. to 10 × 20 cm., although there seemed to be a considerable preference for smaller portals, whenever possible. Chamberlain, Ernst, Lenz, Martin, and Merritt definitely expressed their preference for smaller portals, although it seemed to be the general feeling that portals of about 7 to 8 cm. in diameter are about as small as can be safely used to treat a single lesion at a depth. Smaller portals than this are too difficult to localize and become misdirected if the patient moves even slightly during treatment. Mattick and Widmann had used larger portals in all cases, 10 × 10 cm., 10 × 15 cm., and 10 × 20 cm.

Chamberlain, Lenz, Martin, and Mattick employed at least two opposing lateral portals in practically all cases. Ernst, Merritt, and Widmann had also occasionally used one portal only on the side of the lesion. When two or more portals were used, they were usually treated in rotation, except by Cham-

berlain, who insisted upon daily treatments to each and every portal. Widmann had used various plans, sometimes irradiating one portal on one side for ten consecutive days, and then, either with or without a rest period, giving the portal on the opposite side a series of daily consecutive exposures.

In most cases, two opposing fields had been used, but Ernst and Lenz occasionally employed two contiguous fields on the side of the lesion, in addition to one on the opposite side, so as to cross-fire the site of the primary growth. Martin had used two contiguous fields in some cases for irradiating the maxillary antrum.

Martin recommended circular, rather than square or oblong skin portals. These circular fields are obtained by the use of metal cones varying in size from 6 to 12 cm. in diameter. He discussed his reasons for the use of circular rather than square portals, as follows: The average growth of the pharynx is roughly spherical in shape, and although one diameter may be longer than the other, the direction of the long diameter can seldom be so accurately determined that it will fit in with the long diameter of an oblong portal. Therefore, since tumors must be considered theoretically spherical (rather than square or oblong), a circular portal is more logical. Another reason for the use of a circular, rather than a square portal, is the comparative efficiency or usefulness of the two shapes of skin portals having equal diameters. The surface area of a circular portal is 20 per cent less than a square portal of equal diameter, and being equally efficient, the circular portal should, therefore, conserve the general tolerance. These theories were illustrated by diagrams.

7. Total Dose in Roentgens.—Chamberlain brought up for discussion the method of expressing the total dosage when several skin portals of the neck had been irradiated to cross-fire a pharyngeal lesion. He contended that if the number of roentgens received by the several portals were added to form a grand total, such a figure would be meaningless in attempting to describe the dose of radiation received by the individual case. He recommended that the total dosage be expressed by stating the individual dose in roentgens received by each portal, and its size. This method of expressing dosage was concurred in by all.

Taking a 20- to 30-day treatment period, as

of average length, and a skin portal 7 to 8 cm. in diameter (50 to 60 sq. cm.), as of average size, the most common total dosage was about 3,500 r to each side of the pharynx. A smaller portal, a longer treatment time, unusual tolerance by the patient, or resistance of the disease were considered as reasons for larger doses (above 3,500 r to each side). The converse of the above conditions were indications for smaller doses (below 3,500 r to each side). It was agreed that smaller doses are generally insufficient.

8. *Reactions in the Skin and Mucosa.*—It was generally agreed that marked reactions in the skin and mucosa are essential in order to obtain complete regression in most pharyngeal cancers. Pfahler, in the general discussion, asked for an expression of opinion from the members of the symposium as to what specific degree of radiation reactions should be purposely produced in the skin and mucous membranes of the neck and pharynx in the treatment of pharyngeal cancer by this method. It was generally agreed that in most cases, such reactions did and should go on to an acute blistering or epidermicidal reaction in the skin, and the formation of a pseudo-diphtheritic membrane in the mucosa. Such reactions in the skin and mucosa are quite tender, but are not painful while at rest. They usually heal after from two to four weeks without difficulty.

9. *Anatomical Varieties of Cancer Treated.*—Most of the reports were concerned with the treatment of pharyngeal and laryngeal cancer only, although Mattick reported the use of the method in nasal cancer. Martin reported the extension of its use to growths of the floor of the mouth, paranasal sinuses, nasal cavity, and nasopharynx.

10. *Histologic Varieties of Cancer Treated.*—There was general agreement to the effect that favorable results were to be expected in most pharyngeal and extrinsic laryngeal growths, whatever the histologic type, although as a general rule, well differentiated epitheliomas and adenocarcinomas are less sensitive than the more anaplastic growths. Histologic grading is of presumptive, but not of absolute value in estimating beforehand the response to radiation. It was also definitely pointed out that no case should be excluded from this type of treatment because of its histologic character, if the primary lesion is situated in the pharynx. Pfahler, in the general discussion, was of the opinion that histologic grading is of little value in outlining treatment.

11. *Combination of Interstitial Radium with Divided Doses of External Radiation.*—Ernst and Widmann reported that they had had no permanent results from the combination of interstitial radiation with the divided dose method of external radiation. These two investigators reported that local slough resulted in most cases in which interstitial radiation was used as an adjunct; Lenz emphasized the dangers of radionecrosis, but stated that he had obtained a few successful results by the combination of methods.

Martin and Mattick both reported good results by this combined technic, and stated that they often planned such a combination of methods on beginning the treatment of an individual case. Martin admitted the frequency of local necrosis, but had found seeds of great value for residual disease in the primary lesion, or in neck nodes, and also for neck nodes widely separated from the main skin portal. He stated that he believed necrosis to be a serious complication in the hypopharynx or larynx, but less so in the oral cavity or upper pharynx. He also suggested that by a combination of external and interstitial radiation, less than the maximum doses of either method alone may be successfully employed with a greater margin of safety.

Gendreau, in the general discussion, stated that he believed the exact technic, as published by Coutard (filter, distance, kilovoltage, milliamperage, size of portal, size of daily dose, etc.), should be followed in all cases, if the general technic employed is to be termed the "Coutard method." In the following discussion, it seemed to be the general opinion that Coutard had not settled upon any exact technic, and that although he should be given full credit for his original observations, and the discovery of a new principle in radiation, the best technic of the divided dose or fractional dose principle had not as yet been settled.

COMMUNICATIONS

COMPULSORY HEALTH INSURANCE

The following communication has been received from the Medical Society of the State of New York concerning a matter so pertinent to all physicians that RADIOLOGY is glad to pass it on to its readers.

Albany, N. Y., Feb. 24, 1935: "The acid

test of experience condemns compulsory health insurance schemes wherever they have been tried," stated Dr. Arthur J. Bedell, President of the Medical Society of the State of New York here to-day, in opposing the bill now pending in the State legislature.

"The medical profession disapproves of the proposed law because this method of handling medical care is damaging to the patient and disastrous to the doctor.

"This protest does not mean opposition to the policies of the administration in its recovery efforts or in any other phases of the 'New Deal.' However, physicians as a class are better qualified to speak than any other group, as to the effects of a compulsory health insurance law on the community. The Medical Society of the State of New York, representative of the physicians of the State, rejects the project. It will not work. It will bring to the community conditions quite the opposite of the expectations of its well-wishing proponents."

Dr. Bedell pointed to the utter failure of compulsory health insurance in Germany, where it has been tried for half a century. He said that Gustav Hartz, labor economist of Berlin, and author of several books on Germany's social politics, has analyzed the fallacies of the scheme and exposed to the world the harm, rather than good, that compulsory health insurance has actually produced. Dr. Bedell stated that this report, entitled, "Will America Copy Germany's Mistakes?" will be published in the March 1 issue of the "New York State Journal of Medicine" as translated from the German by the Pennsylvania Self-insurers' Association of Philadelphia.

"Sick insurance," according to the report, "provides the workman with medical attendance free of charge, with medicine and other necessities, and with an allowance. Anyone will at first sight consider this a great blessing for the workman as well as for national health. The reality, however, is far different.

"The insured workman becomes a second-class patient. The mass demand compels a limitation in the use of medicines. Doctors must not prescribe what they consider good for the patient; they are allowed to give only remedies entered in a book of medical regulations for insurance purposes.

"Dread of illness obsesses most people and this has been pressed into a system 'illness made easy' by which the will to be well is strangled. The doctor is consulted a dozen times where once would be sufficient—the insurance pays.

The prescribing of medicine and bandages is desired. When they have been obtained they lie about until they are no longer fit to be used—the insurance pays. Besides, it is nice to get something in return for the premiums paid year in and year out. There is developed a fear of illness which shakes the will for recovery—the best aid to health. Pretenders and hypochondriacs are bred and the use of medicine becomes excessive.

"Medical science has become a cheap article and doctors have given up conscientious treatment. The genuine patient is neglected, is not given the necessary care. The greater the mass consultation, the lower are the doctor's fees. They are, therefore, compelled to resort to mass practice.

"All this is at the workman's expense, for the part of the premiums supposed to be paid by the employer is in reality borne by the workman either as a consumer or wage earner. As the employer's premium share is immediately connected with the wage, it is shifted over on the wage. In Germany, no one any longer doubts the fact that the employer's share of the premium is taken from the workman's wages. What the employer pays as his contribution, he cannot pay the workman in the form of wages.

"A network of deception has been spread. In millions of cases wrong was turned into right and the gates opened wide to fraud. When wages are being decreased, when work is scarce, and work hours shortened, when there are fewer shifts, many holidays, sick insurance comes in handy. One objects to the work he is given, another does not feel like working. Matters soon make an extensive controlling system necessary. This ends in badgering all persons.

"Patients are visited in their homes by controlling officials who have to convince themselves that the patient is really ill and not doing any work. The sick insurance engages so-called confidential doctors who have to submit the patient to a final examination to see whether he is too ill to work. The results of such examinations are to a great extent startling. Here is one instance from among thousands: 2,008 patients were ordered to appear for a final examination: 816 of them at once declared their complete recovery; 289 were found to be well by the confidential doctor. So nearly half of them were not ill at all.

"The confidential doctor is, so to say, the medical policeman, who not only controls the patients but also his fellow-doctors who are treating them.

"The genuine patient is justly indignant to find that the existence of his illness is doubted, and that he who has always paid his premiums regularly and has a right to demand conscientious attendance, is considered a cheat.

"This system, together with the rest of the bureaucratic apparatus, has wedged itself between doctor and patient, completely destroying the patient's confidence in his physician, which greatly retards all recovery.

"Those who know anything about the actual working of compulsory health insurance will not be surprised that the confidential doctor, whose task it is to keep the number of patients low, may declare a patient recovered, who nevertheless dies two days later."

FEE TABLES AND THE ROENTGENOLOGISTS¹

By EMMET KEATING, M.D., *Chicago*

The Chicago Roentgen Society has a disturbing problem which is partly a manifestation of this changing world, but which is mostly a misapprehension on the part of the medical profession as to the status of a roentgenologist.

For several years the profession has been in receipt of published fee tables from both x-ray and clinical laboratories. Physicians have never questioned the custom but rather have been inclined to regard it with favor. It makes it convenient for them to answer questions of patients relative to the cost of the work the physician wishes to have done. The custom practically sets an arbitrary price that must be met by all laboratories and does not take into account the ability of the roentgenologists to perform the work. The problem of the roentgenologist is further complicated by hospital competition. Hospitals must have x-ray departments and should also have the best that there is in the way of a roentgenologist.

It is most unfortunate that many physicians consider the roentgenologist a mere photographer. Some of them are. All of the competent men in that specialty resent the implication but to no avail. It is a sentiment as deeply rooted in the minds of the profession as is the belief on the part of the laity that the best doctors are the ones who have the greatest number of patients. The roentgenologists

know how this misconception on the part of the profession can be set right, but they are too modest to suggest the way out of the humiliating situation in which they find themselves.

No self-respecting physician would refer a patient to an ophthalmologist who would prescribe glasses when glasses are not needed. Neither is a physician humiliated when an ophthalmologist tells the patient that glasses are unnecessary. The patient is perfectly satisfied to pay the ophthalmologist a fee for his advice and the family doctor has not suffered from loss of confidence on the part of the patient. This well-established attitude held by the public, the family doctor, and the ophthalmologist is due to the fact that none of the parties concerned think of the ophthalmologist in terms of a set of trial lenses. The ophthalmologist is considered a capable physician who has confined his work to the care of the eyes. Because of the imposing magnitude of the x-ray machine, the roentgenologist, as a learned physician, is over-shadowed and lost to view.

The roentgenologists are expected to take the picture or pictures indicated by the family doctor. They are not supposed to question the referring doctor's opinion as to what part of the body should or should not be x-rayed. Many a patient with heart disease, not discovered by the attending physician, is sent to the roentgenologist with instructions to make a complete gastro-intestinal radiological study that is entirely unnecessary. If the roentgenologist dared to assert himself, the family doctor would receive an x-ray picture of the chest, with the accompanying report, and a frank and fearless statement of there being no indications for doing a gastro-intestinal series.

I believe that in all cases, other than minor fractures, the attending physician should furnish the roentgenologist with a careful history of the patient and the roentgenologist should make a partial physical examination that will enable him to judge what pictures should or should not be made. If this is done, the number of unnecessary pictures at present being taken will be greatly reduced.

The charge by the roentgenologist should be made on exactly the same basis as that of any other physician, namely, the time and the skill required and the ability of the patient to pay. Roentgenologists are most co-operative in this respect, and physicians should restrain them-

¹ Reprinted from the "Chicago Medical Society Bulletin," Jan. 26, 1935.

selves from looking for x-ray bargains in order to save the patient a few dollars. The attending physician is the best judge of the patient's ability to pay and it is his duty to impart this information to the roentgenologist.

It might be a good plan if at least once a year, a meeting of the Chicago Medical Society were devoted to discussion of what is a reasonable fee. There are many physicians whose estimates are too low, while, on the other hand, there are some physicians who obtain fees from comparatively poor people that are entirely out of proportion to the service rendered. Practices of that kind are often responsible for the lay opinion of the medical profession that was recently expressed by Mr. O'Brien in his column in the *Chicago Daily News*.

It should not be difficult to understand that if physicians will consider the roentgenologist in the same light they consider the ophthalmologist or the otolaryngologist, the problem now confronting the roentgenologists will be solved. The sending of fee tables will be evidence that the sender brands himself as one who renders an inferior service.

DOSAGE FACTORS

Roentgenologists doing therapy are urged to familiarize themselves with the Recommendations of the International Committee for Radiological Units (see *RADIOLOGY*, November, 1934, 23, 580), to the end that reported results may be reproducible by others. The advantages to be derived from the use of a uniform technic, such as may be reported in dosage factors known to all, are manifest. Follows a list of those factors which should be recorded in reporting therapy results, and which one needs to know in order to follow the successful courses of others.

- (1) Number of roentgens (r) delivered to each treatment area (measured in free air).
- (2) Dosage rate (rate of applying the radiation, r/min.).
- (3) Equivalent voltage.
- (4) Filter—material and thickness (also include approximate tube wall thickness).
- (5) Distance (skin to target).
- (6) Interval between irradiations.
- (7) Size and number of ports of entry.

In this connection, therapists are referred to the Report of the Committee on Standardization of X-ray Measurements in *RADIOLOGY*, March, 1934, 22, 289.

ANNOUNCEMENTS

ANNUAL MEETING, 1935

The Executive Committee have chosen Detroit, Michigan, for the 1935 meeting place of the Radiological Society of North America. The meeting will be held in the Hotel Statler, December 2 to 6, 1935.

PAN-AMERICAN MEDICAL ASSOCIATION'S CRUISE FOR 1935

The S. S. *Columbia*, the largest American cruise ship afloat—40,000 tons, with three swimming pools and a sand beach on deck—has been selected by the officials of the Pan-American Medical Association for the cruise. The ship will sail from New York on July 18, returning to New York on August 28. The itinerary will be as follows: New York, Havana, Curaçao, five days at Rio de Janeiro (where a scientific congress will be held), three days at Santos (for attending a scientific convention at Sao Paulo), Trinidad, Santo Domingo, Kingston (Jamaica), Havana, and New York.

Accommodations per person are from \$450.00 up, which is as low as \$11.00 a day.

This will be an unusual opportunity to combine a wonderful vacation with recreation, education, good fellowship, and good health. The Section on Radiology is one of the live members of the Association. Its President is Frederick W. O'Brien, M.D., 465 Beacon St., Boston, Mass., who invites you to contribute some article on radiology. Please say that you will go, and send in your title within thirty days, if possible.

For further particulars of the cruise, write to the Director-General, Joseph J. Eller, M.D., 745 Fifth Avenue, New York City.

ALBERT SOILAND, M.D.
Chairman Executive Committee,
Section of Radiology

PAN-AMERICAN MEDICAL ASSOCIATION

The Sessions of this Association have proven to be of great scientific value, while the fellowship of leading spirits in all specialties of medicine has resulted in a better understanding and mutual respect. Under the leadership of Frederick W. O'Brien, M.D., President of the

Section on Radiology for North America, and of Albert Soiland, M.D., Chairman of the Executive Committee for North America, the interests of radiology will be ably taken care of.

The officers for North America are: Chevalier Jackson, M.D., of Philadelphia, *President*; Harlow Brooks, M.D., of New York City, in charge of the Surgical Division; Lewellys F. Barker, M.D., of Baltimore, in charge of the Medical Division; Charles H. Mayo, M.D., of Rochester, Minn., among the Vice-presidents; Hugh H. Young, M.D., of Baltimore, in charge of the Genito-urinary Section; Douglas Quick, M.D., of New York City, in charge of the Section on Neoplastic Diseases.

The officers of the Executive Committee for the Section on Radiology are as follows: *President*: Frederick W. O'Brien, M.D.; *Vice-presidents*: Leon J. Menville, M.D., B. R. Kirklin, M.D., Edwin C. Ernst, M.D., Byron H. Jackson, M.D., Edward W. Chamberlain, M.D.; *Secretary*: John Sproull, M.D.; *Executive Committee*: Albert Soiland, M.D., George E. Pfahler, M.D., George W. Grier, M.D., Ernst A. May, M.D., Amédée Granger, M.D., Harry M. Imboden, M.D., and Benjamin H. Orndoff, M.D.

AN AWARD

A David Anderson-Berry Gold Medal, together with a sum of money amounting to about £100, will be awarded in July, 1935, by the Royal Society of Edinburgh to the person, who, in the opinion of the Council, has recently

produced the best work on the nature of x-rays in their therapeutic effect on human diseases. A similar award will be made every three years.

WILLIAM DUANE

IN MEMORIAM

We are deeply grieved to announce the recent death of Dr. William Duane, of Philadelphia, one of the world's best known physicists, who has done so much for advancing the science of radiology.

Dr. Duane was born in Philadelphia in 1872. He received his A.B. degree from the University of Pennsylvania in 1892; in 1893 he also received an A.B. degree from Harvard University; his Ph.D. degree was obtained from the University of Berlin, Germany; in 1922 the honorary degree of Doctor of Sciences was conferred by the University of Pennsylvania. He was a member of the Cancer Commission of Harvard University and Research Fellow since 1913. He served on the international committee for the establishment of the r-unit. Among his numerous contributions to science, his work on the x-ray spectra of light elements has given him world-wide publicity.

The Radiological Society of North America and the Journal RADIOLOGY mourn Dr. Duane. He was an Honorary Member of the Radiological Society of North America and received the Society's Diploma.

His loss will be felt by many, but surely none could feel his loss greater than the radiologists of this and other countries for whom he has done so much.

BOOK REVIEW

THE HEART VISIBLE: A CLINICAL STUDY IN CARDIOVASCULAR ROENTGENOLOGY IN HEALTH AND DISEASE. By J. POLEVSKI, M.D., attending physician and cardiologist, Newark Beth Israel Hospital. Published by F. A. Davis Co., Philadelphia, 1934. A volume of 207 pages, with 122 illustrations. Price: \$5.00.

The crying need for an English-language monograph on the roentgen examination of the heart and great vessels is evident to any one who has had any contact with this field. This small book is, therefore, welcome, in spite of the disappointment occasioned by the inadequacy of its treatment of the subject. If it be assumed that it is intended for students and clinicians who are relatively unfamiliar with roentgen methods, it may well fulfill its purposes; it is doubtful, however, whether it will be very helpful to the mature roentgenologist. When an author discusses a circumscribed subject, such as this one, it does not seem unreasonable to expect that it be considered completely. There is an immense literature in this field, and numerous volumes concerned with it have appeared both in German and French; the opportunity to present accurate and detailed information on every phase of the matter is thus readily afforded. The effort to compress the text into a small space defeats the very purpose of any reference book, and in this instance prevents complete fulfillment of this opportunity.

The book contains 183 pages of text and is well printed and well illustrated. Certain sections, such as that on the pathologic physiology of mitral disease and on the effects of extrinsic factors on the heart, are very well presented. On the other hand, the discussion of the methods of examination and their relative value is much too brief. Certainly the

measurement of cardiac area and its relation to height and weight is dismissed too casually.

The actual errors are relatively infrequent although attention should be directed to a few of the more prominent ones. The statement that the third curve on the left border of the heart is due to the left atrium or its appendage should at least have been qualified, if the author was unwilling to accept the recent refutations of this oft-repeated error. Likewise the statement that enlargements of the right ventricle can hardly be seen in postero-anterior views is probably incorrect. In fact, the author's own consideration of the enlargement of the heart in mitral disease tends to disprove both of these propositions.

The omissions are much more numerous, and a few of the more glaring ones may be noted. The use of diagrammatic cross-sections would clarify the section on anatomical relations. There is no mention whatever of the roentgenoscopic findings in pericardial effusion, and the treatment of this condition is most inadequate. There is no reference to the roentgen observation of calcification of the valves of the heart or of the coronary arteries. There is an implied pessimism as to the roentgen diagnosis of aortic aneurysm which is hardly justified. No mention is made of aneurysms of the ascending aorta extending to the left, and the effects of aneurysms on the esophagus are hardly considered. The many valid objections to the Kreuzfuchs method of measurement of the aortic arch are not brought out, giving a somewhat false idea of the value of the method. There is a rather insufficient discussion of the differential diagnosis of various heart conditions.

The author has presented his material attractively and the errors are insufficient to detract from the value of the book. It may well be recommended as an introduction to the study of the roentgen diagnosis of cardiovascular disease.

ABSTRACTS OF CURRENT LITERATURE

CONTENTS BY SUBJECT

Agranulocytosis.....	376	Inflammatory Diseases.....	382
The Appendix.....	376	The Kidneys.....	383
Bone Diseases (Diagnosis).....	376	Knee Joint.....	383
Calculi.....	377	The Lungs.....	383
Cancer (Diagnosis).....	377	The Mastoids.....	385
Cancer (Therapy).....	377	Peptic Ulcer (Diagnosis).....	385
Contrast Media.....	378	Pleurisy, Mediastinal.....	386
Cosmic Rays.....	379	The Prostate.....	386
Dosage.....	379	Radiation Effects.....	386
Eye (Therapy).....	379	Radium.....	386
The Foot.....	379	Roentgen Sickness.....	386
Fractures.....	379	The Stomach.....	387
Gall Bladder (Normal and Pathologic).....	379	Tuberculosis, Intestinal.....	387
Gas Gangrene.....	380	Tuberculosis, Pulmonary.....	388
Gastro-intestinal Tract (Diagnosis).....	380	Tumors (Diagnosis).....	389
Genito-urinary Tract (Diagnosis).....	382	Tumors (Therapy).....	389
Grenz Rays.....	382	The Uterus.....	390
Hemophilia.....	382	The Wrist.....	390

THE FOLLOWING ABSTRACTORS HAVE CONTRIBUTED TO THIS ISSUE

J. N. ANÉ, M.D., of New Orleans
S. M. ATKINS, M.D., of Waterbury, Connecticut
J. E. HABBE, M.D., of Milwaukee
HANS W. HEFKE, M.D., of Milwaukee

DAVIS H. PARDOLL, M.D., of Chicago
E. A. POHLE, M.D., Ph.D., of Madison, Wisconsin
CHARLES G. SUTHERLAND, M.D., of Rochester, Minn.

CONTENTS OF ABSTRACTS IN THIS ISSUE LISTED ALPHABETICALLY BY AUTHORS

BADER, A., with LUDIN, M., jt. auth.....	379	GERSHON-COHEN, JACOB, with BOLES, RUSSELL L., jt. auth.....	387
BARNEY, J. D., and MINTZ, E. R. Some Newer Conceptions of Urinary Stone Formation.....	377	GLASS, AMEL. The Bronchopulmonary Segment, with Special Reference to Putrid Lung Abscess.....	385
BARSONY, T., and WINKLER, K. Paget's Disease as an Accidental Finding.....	376	GOLDHAMER, K. Roentgen Therapy of Bone Sarcoma.....	389
BENJAMIN, JULIEN E., and BIEDERMAN, JOSEPH B. Agranulocytic Leukopenia: Report of a Case Successfully Treated with X-rays, and Some Observations on the Effect of Amidopyrine.....	376	GUTIG, C., and HERZOG, A. Polyposis in the Entire Gastro-intestinal Tract.....	381
BERGH, G. S., with IVY, A. C., jt. auth.....	379	HARRINGTON, FRANCIS E., with MYERS, J. ARTHUR, jt. auth.....	388
BIEDERMAN, JOSEPH B., with BENJAMIN, JULIEN E., jt. auth.....	376	HELD, A., and HULBACH, H. The Fibrinogen Content of the Blood under the Influence of Roentgen Irradiation and the Primary Effect of Radiation.....	386
BOLES, RUSSELL L., and GERSHON-COHEN, JACOB. Intestinal Tuberculosis: Pathologic and Roentgenologic Observations.....	387	HERZOG, A., with GUTIG, C., jt. auth.....	381
BRUCK, SAMUEL. Round Foci Type of Pulmonary Tuberculosis.....	388	HOHENNER, KARL. The Early Diagnosis of Carcinoma of the Small Intestine.....	377
BRUNN, HAROLD. Lung Abscess.....	383	HULBACH, H., with HELD, A., jt. auth.....	386
CANIGIANI, T., and SINGER, K. The Differential Diagnosis of Osteitis Deformans (Paget's Disease) and Syphilis of the Bone.....	376	HUMMEL, RUDOLF. Two Cases of Juvenile Osteitis Deformans Paget.....	377
DE LORIMIER, ALFRED A., with MOORE, JOHN J., jt. auth.....	376	IVY, A. C., and BERGH, G. S. The Applied Physiology of the Extra-hepatic Biliary Tract.....	379
DIXON, CLAUDE E. Carcinoma of the Cecum: What Are the Chances for Cure?.....	378	JORDAN, SARA M., and KIEFER, EVERETT D. Complications of Peptic Ulcer: Their Prognostic Significance.....	385
ENGELSTAD, R. B. Have Cosmic Rays Demonstrable Biologic Effects?.....	379	KIEFER, EVERETT D., with JORDAN, SARA M., jt. auth.....	385
FARINAS, PEDRO L. Serial Bronchography for the Diagnosis of Purulent Diseases of the Lungs.....	384	KLOVEKORN, G. H. Epilation of Rabbit Skin Following Irradiation.....	386
FELDMAN, MAURICE, with FRIEDENWALD, JULIUS, jt. auth.....	380	KOCH, F. Biologic Experiments with Grenz Rays.....	382
FELSEN, JOSEPH. The Pathological Appendix.....	376	KRAUS, LEONARD. The Roentgenologic Diagnosis of Mastoiditis.....	385
FERGUSON, RUSSELL S. Studies in the Diagnosis and Treatment of Teratome Testis.....	389	KREMSEK, KURT. Multiple Diverticula in the Cardiac End of the Stomach.....	387
FRIEDENWALD, JULIUS, and FELDMAN, MAURICE. The Unstable or Irritable Duodenum: Clinical Observations in 100 Cases.....	380	KRUGLIKOWA, R. K., and WEISSBLATT, S. N. Roentgen Therapy in Acute Inflammatory Diseases of the Mouth.....	382
GEORGE, ARIAL W., and LEONARD, RALPH D. Ununited Intracapsular Fractures of the Femoral Neck Roentgenographically Considered.....	379	KUHN, HERMANN. "Peremesin" for the Prevention of X-ray Sickness.....	386
		KURATSCHENKOW, A. J. The Treatment of Erosions of the Uterus with Roentgen and Radium Rays.....	390

- LANG, A. Radium Therapy in Malignant Tumors of the Upper Respiratory Tract: Results Based on Five Years' Observations. . . . 386
- LEONARD, RALPH D., with GEORGE, ARIAL W., jt. auth. . . . 379
- LEVIN, ALFRED G., with SWENSON, PAUL C., jt. auth. . . . 378
- LEVINE, SAMUEL, with SOLIS-COHEN, LEON, jt. auth. . . . 382
- LUDIN, M., and BADER, A. Roentgen Therapy of a Post-traumatic Cyst of the Iris. . . . 379
- MESTERN, JURGEN. Hereditary Synostoses of the Small Bones of the Hand and Foot: Hereditary *os tibiale externum*. . . . 390
- MINTZ, E. R., with BARNEY, J. D., jt. auth. . . . 377
- MOORE, JOHN J., and DE LORIMIER, ALFRED A. Roentgenographic Studies of Parathyroid Deossification. . . . 376
- MURPHY, J. E. Bronchography, an Essential and Safe Adjunct in the Study of Pulmonary Tuberculosis. . . . 388
- MYERS, J. ARTHUR, and HARRINGTON, FRANCIS E. The Effect of Initial Tuberculous Infection on Subsequent Tuberculous Lesions. . . . 388
- NEEFF, T. C. Advances in the Standardization of Practical Dosage in Roentgen and Radium Therapy. . . . 379
- OBERHOLZER, J. Pneumoradiograms of the Knee Joint. . . . 383
- PFÄHLER, GEORGE E. Roentgen Diagnosis of Mediastinal Tumors and Their Differentiation. . . . 389
- PINNER, MAX. Hematogenous (Non-miliary) Pulmonary Tuberculosis. . . . 388
- POHLE, ERNST A., and RITCHIE, GORTON. Histological Studies of the Liver, Spleen, and Bone Marrow in Rabbits Following the Intravenous Injection of Thorium Dioxide. . . . 378
- POPP, L. A Case of Sarcoma of the Prostate Cured by Roentgen Therapy. . . . 386
- POTTER, B. P. Bronchography in Relation to the Pathology of Pulmonary Tuberculosis. . . . 388
- PREVOT, R. The Roentgen Diagnosis of Intermittent Ileus. . . . 381
- QUICK, DOUGLAS. Management of Cancer of the Mouth and the Cervical Lymphatics. . . . 377
- REHFUSS, MARTIN E. Proteins *versus* the Carbohydrates: An Inquiry into their Gastric Digestion. . . . 381
- REIPRICH, W. Results in the Treatment of Carcinoma of the Cervix by the Women's Clinic of the University of Breslau. . . . 390
- RITCHIE, GORTON, with POHLE, ERNST A., jt. auth. . . . 378
- ROSE, D. K. Postpartum Pyelitis of Pregnancy: Treatment of Certain Cases without the Use of the Ureteral Catheter: Explanation Based on Physiology of the Bladder. . . . 382
- SCHOONOVER, JANETTA WRIGHT, SHIELS, ETHOL HALL, and WIDMANN, BERNARD P. Alterations in the PH of the Blood in Cancer Following Roentgen and Gamma Irradiation. . . . 378
- SCHNEIDER, JUSTUS. The Importance of Roentgenologic Examination for the Diagnosis and Treatment of Gas Gangrene of an Extremity. . . . 380
- SEARS, NATHAN P. Treatment of Unilateral Urinary Fistulas by X-ray Destruction of the Kidney: A Clinical and Experimental Study. . . . 383
- SHIELS, ETHOL HALL, with SCHOONOVER, JANETTA WRIGHT, jt. auth. . . . 378
- SIMONSEN, MARTIN. Benign Tumors of the Stomach. . . . 387
- SINGER, K., with CANIGIANI, T., jt. auth. . . . 376
- SOLIS-COHEN, LEON, and LEVINE, SAMUEL. Bone and Joint Changes in Hemophilia. . . . 382
- SPITZENBERGER, O. The Diagnosis of Lymphosarcoma of the Stomach. . . . 387
- SWENSON, PAUL C., and LEVIN, ALFRED G. Primary Carcinoma of the Duodenum: Case Report. . . . 378
- UDVARDY, LADISLAUS. Round Shadows in the Lungs. . . . 384
- UDVARDY, LADISLAUS. Mediastinal Pleurisy. . . . 386
- WEISSBLATT, S. N., with KRUGLIKOWA, R. K., jt. auth. . . . 382
- WIDMANN, BERNARD P., with SCHOONOVER, JANETTA WRIGHT, jt. auth. . . . 378
- WINKLER, K., with BARSONY, T., jt. auth. . . . 376
- ZEITLIN, A. Unilateral Periosteal Thickening of the Metatarsals. . . . 379
- ZIMMER, EMIL A. Gallstones and their Diagnosis in a Gall Bladder not Filled by Dye. . . . 380

AGRANULOCYTOSIS

Agranulocytic Leukopenia: Report of a Case Successfully Treated with X-rays, and Some Observations on the Effect of Amidopyrine. Julien E. Benjamin and Joseph B. Biederman. *Jour. Am. Med. Assn.*, July 21, 1934, 103, 161-163.

Severe and repeated attacks of agranulocytosis have been reported as early as 1931 in an individual using large amounts of coal tar derivatives. Kracke suggested that the benzene chain contained in the drugs might act as a powerful leukocytic depressant.

The authors report a severe granulopenia, the result apparently of self-medication with amidopyrine. The patient was immediately given high voltage roentgen therapy over the long bones and the effect was most impressive. There was a prompt alleviation of the severe aching, the fever gradually receded, and there was an early restoration of the white count to normal standards. The patient had several attacks, all associated with the use of one of the coal tar derivatives. All were amenable to roentgen therapy. The patient was shown to have an idiosyncrasy to amidopyrine.

CHARLES G. SUTHERLAND, M.D.

THE APPENDIX

The Pathological Appendix. Joseph Felsen. *Am. Jour. Roentgenol. and Rad. Ther.*, March, 1934, 31, 340-345.

This article is concerned with the correlation of the clinical and microscopic findings of various types of appendiceal pathology as compared with the radiographic appearance of the barium-filled appendix determined immediately after surgical removal, the appendix being carefully filled with a heavy suspension of barium in 5 per cent formalin. In the early acute lesion the wall shows slight thickening, while the canal presents a saw-tooth or stalactite appearance. In the late acute, the wall is thickened or perforated, while the canal shows stenosis or widening. The chronic or healed case shows a thickened or atrophic wall, with widening stenosis, or obliteration of the lumen.

J. E. HABBE, M.D.

BONE DISEASES (DIAGNOSIS)

The Differential Diagnosis of Osteitis Deformans (Paget's Disease) and Syphilis of the Bone. T. Canigiani and K. Singer. *Röntgenpraxis*, August, 1934, 6, 509-512.

Paget's disease and syphilis of the bone are sometimes impossible of differentiation both clinically and roentgenologically. The case described by the authors showed a marked sclerosis of the shaft of the right femur, definite widening, periosteal thickening, and a coarse structure of the medulla, with formation of cysts. The other bones were negative. The diagnosis of Paget's disease was made, but in consideration of the irregular thickening of the periosteum, the localization of the process in the diaphyses, without involvement of the ends of the bone, and the absence of pathology of other bones, the diagnosis was changed to diffuse syphilitic osteitis. A biopsy showed changes typical

of Paget's disease. The patient, however, became much improved after anti-syphilitic treatment, and the authors believe that syphilis was the correct diagnosis.

HANS W. HEFKE, M.D.

Paget's Disease as an Accidental Finding. T. Bársony and K. Winkler. *Röntgenpraxis*, November, 1934, 6, 730-734.

Paget's disease is much more common than one heretofore has believed. In Schmorl's pathologic institute it was found in 2.75 per cent of the patients. Several cases of unsuspected Paget's disease are reported, in some of which only one or only a few bones were attacked. In the highest percentage of cases, the vertebrae and sacrum were involved, but there was also a localized osteitis deformans in the clavicle.

The frequency of Paget's disease in living patients needs to be determined because there is a great discrepancy between roentgenologic and pathologic percentages. The matters of age and first findings of Paget's disease have to be investigated. The question of sarcomatous degeneration has yet to be settled. Some authors believe that it takes place in about 2 per cent of the cases, but this percentage is probably too high. Early diagnosis is possible only by roentgen examination, and a trial of roentgen therapy might be indicated if the lesion is confined to one bone.

HANS W. HEFKE, M.D.

Roentgenographic Studies of Parathyroid Deossification. John J. Moore and Alfred A. de Lorimier. *Am. Jour. Roentgenol. and Rad. Ther.*, April, 1934, 31, 496-511.

Deossification was studied experimentally under varied conditions, namely, parathormone administration, ammonium chloride (acid), sodium bicarbonate (alkali), relation of either acid balance or alkaline balance to parathormone effect, thyroid extract, and disuse atrophy. Clinically observed manifestations of deossification were applied to osteitis fibrosa, multiple benign giant-cell tumors, and osteitis deformans.

The state of osseous metabolism is conspicuously manifested in the metaphyseal regions of the long bones. A thyroid extract and acid balance regimen was seen to synergize the effects of parathormone, and independently each was seen to effect a marked increase in the inorganic phosphorus excretions. Sodium bicarbonate was seen to inhibit the action of parathormone, as suggested by biochemical studies of Stewart and Haldane.

Reossification was observed after imposing a high calcium intake plus a relatively alkaline balance.

Clinically, the manifestations of progressive deossification are emphasized by a multiplicity of osseous dissolutions—cases of osteitis fibrosa or multiple cystic formations and cases of multiple benign giant-cell tumors. Closely related would seem to be those cases manifesting reossifications—such as osteitis deformans. In extreme cases of the latter there would appear to have occurred alternate deossifications and reossifications—in some cases, perhaps, a cyclical hyperparathyroidism.

S. M. ATKINS, M.D.

Two Cases of Juvenile Osteitis Deformans Paget. Rudolf Hummel. *Röntgenpraxis*, August, 1934, 6, 512-519.

Schmorl did not see any cases of Paget's disease in patients under 40 years of age in his large autoptic material. There have been reports of cases under 30 years of age in the literature. The author reports two cases in children, 11 and 9 years of age.

In the first case the right femur showed the typical roentgenologic appearance of Paget's disease with a pathologic fracture. The pelvis was also involved. The boy was seen several times during the course of five years, with pathologic fractures. A biopsy proved the diagnosis of osteitis deformans Paget.

The second case (9 years) was not proved by biopsy, but showed typical sclerosis and deformities in the pelvis, femora, and other bones.

The formation of callus took place in a normal way in both cases. X-ray therapy was tried in one patient with no benefit.

HANS W. HEFKE, M.D.

CALCULI

Some Newer Conceptions of Urinary Stone Formation. J. D. Barney and E. R. Mintz. *Jour. Am. Med. Assn.*, Sept. 8, 1934, 103, 741-743.

These authors discuss the association of hyperparathyroid disease and renal calculi. If hyperparathyroidism is in the nature of an endocrine dysfunction, it must be generalized throughout the body and the urinary tract. Why, then, does it not result in stones in all cases or in bilateral stones uniformly? The fact that it does not would indicate that there must be some still unknown factor at work in the kidney itself which prevents stone formation in certain cases. By the same reasoning, there must be a local renal factor that induces unilateral stone in certain individuals and bilateral stones in others. Perhaps a still more intensive study of the colloids will supply the answer. Possibly dietary and vitamin deficiencies or errors will be found to play a part more than seems now to be the case. Also it may be possible that infection or even stasis will come to be regarded more seriously. That some disturbance of metabolism, plus a factor or factors existing at least temporarily in one or both kidneys, is at work seems a plausible working hypothesis. The realization that hyperparathyroidism will account for at least a part of the problem is important and encouraging. Further studies by the endocrinologist and the biochemist, as well as by the physiologist, will eventually succeed in solving the question of urinary stone formation.

CHARLES G. SUTHERLAND, M.D.

CANCER (DIAGNOSIS)

The Early Diagnosis of Carcinoma of the Small Intestine. Karl Hohenner. *Röntgenpraxis*, October, 1934, 6, 677-679.

There is only one method which allows the diagnosis

of malignant infiltration in the small intestine before the appearance of symptoms of obstruction: the roentgenologic examination. A case is described in which a carcinoma was diagnosed roentgenologically at a relatively early stage. The diagnosis was possible by a break in the mucosal folds, without dilatation of the involved portion of the intestine. It is interesting to note that the patient had had an exploratory laparotomy two weeks before the roentgenologic examination at which the tumor had not been found.

HANS W. HEFKE, M.D.

CANCER (THERAPY)

Management of Cancer of the Mouth and the Cervical Lymphatics. Douglas Quick. *Am. Jour. Roentgenol. and Rad. Ther.*, March, 1934, 31, 366-377.

Treatment of intra-oral cancer embraces the primary growth and the usual paths of metastasis. Intra-oral cancer includes epidermoid carcinoma of the oral mucosa, maxillary antrum, and structures of the tonsillar fossa.

Treatment of Primary Tumor.—External irradiation is best. A few may yield completely to this method alone; usually there is regression only, and treatment must be completed by interstitial irradiation. For surface irradiation, radium has no place. For interstitial irradiation, radon seeds are best, especially in gold capillary tubes. With proper technic, necrosis is rare.

The influence of tumor histology is not as great in this class as in others but valuable, nevertheless. Grades III and IV, except in the tonsil, are rare. Relatively few are anaplastic. In the tonsil group, many are anaplastic and external irradiation only is indicated. Oral hygiene is very important, even if, to accomplish it, it is necessary to hospitalize the patient. Feeding must be kept up, with a nasal tube, if necessary. When syphilis is present as a complicating factor, the cancer is treated first gently; later, when it has been controlled, it may be treated in the usual fashion. If necessary, a cautery is used—for access to the tumor-bearing area, to produce drainage, or when there is invasion of bone. In the antrum the anterior wall and adjacent alveolar process is removed for implantation of the seeds. In the floor of the mouth, implantation is made first, before cautery removal of diseased tissue. This includes osteomyelitis of bone or revision of the scar in the syphilitic area, or any scar that threatens to break down or produce deformity.

Treatment of the Cervical Lymph Nodes (Metastatic or Uninvolved).—Dissection *en bloc* is now not indicated, especially on account of its limitations and the better results produced with radiation therapy. Anaplastic epidermoid carcinoma is controlled or destroyed completely by external radiation alone. Complete and partial undifferentiated growths tend to widespread distribution and multiple metastasis early in their course, like glandular types of cancer.

Complete unilateral neck dissection should be re-

served for fully differentiated epidermoid carcinoma in patients of good general physical condition, with primary growths controlled, and in whom the metastatic nodes are unilateral, palpable, and have an intact capsule. A review of the material indicates that if dissection is to be done, it should be most radical, except in cases of lip carcinoma. Removal of both submental groups and the submaxillary and upper deep cervicals on the involved side is as good as the complete operation.

Influence of Histology.—This is an outstanding guide to the procedure to be followed.

S. M. ATKINS, M.D.

Primary Carcinoma of the Duodenum: Case Report. Paul C. Swenson and Alfred G. Levin. *Am. Jour. Roentgenol. and Rad. Ther.*, February, 1934, **31**, 204-207.

The authors report a case of a man, aged 59, who was first examined after a period of three months during which he had suffered vague upper abdominal pain and general weakness, with a weight loss of 15 pounds. A malignancy of the gastro-intestinal tract was suspected although the physical findings were entirely negative. Gastro-intestinal x-ray examination was reported to be entirely negative, but upon review of the films at a subsequent date an alteration of the mucosal pattern in the descending portion of the duodenum was seen. The patient was moderately anemic at this time.

When re-examined 13 months later he showed a jaundice of two weeks' duration, and a firm rounded mass was palpable in the right upper abdomen. X-ray studies showed a filling defect of the second portion of the duodenum, without any five-hour gastric retention. The diagnosis was carcinoma of the common bile duct or the duodenum. At operation a mass 10 cm. in diameter was palpated near the head of the pancreas. Cholecystostomy was done, but the patient died the third day after operation. At necropsy a tumor measuring 6.5 by 7 cm. was found in the second portion of the duodenum, with the ampulla of Vater being located almost in the center of the tumor. There was no extension beyond the limits of the duodenal wall. Microscopic examination showed adenocarcinoma or a high cuboidal and columnar epithelial type, forming irregular acini, and apparently arising from the mucosa of the duodenum.

J. E. HABBE, M.D.

Alterations in the PH of the Blood in Cancer Following Roentgen and Gamma Irradiation. Janetta Wright Schoonover, Ethol Hall Shiels, and Bernard P. Widmann. *Am. Jour. Roentgenol. and Rad. Ther.*, April, 1934, **31**, 532-537.

There is no definite trend in PH during a course of radiation therapy.

Roentgen irradiation of uncomplicated cases, with and without cancer, is followed by a slight acid change in the PH of the blood within an hour of treatment; roentgen irradiation of complicated cancer cases is followed by alterations of less consistency, but with a slight alkalotic trend.

The alteration within an hour of roentgen irradiation disappears within twenty-four hours.

Gamma irradiation is followed by a definite alkalotic tendency, more marked just before the removal of the radon application than afterward; this alkalosis is considerably reduced after roentgen irradiation.

S. M. ATKINS, M.D.

Carcinoma of the Cecum: What Are the Chances for Cure? Claude E. Dixon. *Jour. Am. Med. Assn.*, Nov. 24, 1934, **103**, 1605-1607.

Some persons apparently are inherently susceptible to the development of malignant processes. Examples are the multiple carcinomas, each of a distinctly different type, occurring simultaneously or consecutively in the same patient.

Malignant lesions of the colon, for the most part, are single (except those which apparently arise from malignant degeneration accompanying multiple polyposis). Radical removal is the most effective means of relief. Growths in this segment of the bowel may reach considerable size without the appearance of the phenomena of obstruction. The vast majority of cases show an anemia. Growths occurring in or involving the ileocecal valve usually produce sufficient dyspeptic symptoms, from obstruction, to make the diagnosis relatively easy. Those in which a mass is palpable are usually discovered by accident.

Prognosis varies with the grade of malignancy and the occurrence of metastases. Involvement of lymph glands was found in 25 per cent of the author's series of 60 cases that had survived from five to something over twenty-two years after operation.

CHARLES G. SUTHERLAND, M.D.

CONTRAST MEDIA

Histological Studies of the Liver, Spleen, and Bone Marrow in Rabbits Following the Intravenous Injection of Thorium Dioxide. Ernst A. Pohle and Gorton Ritchie. *Am. Jour. Roentgenol. and Rad. Ther.*, April, 1934, **31**, 512-519.

This is a report of a study of 80 rabbits for observation periods up to 493 days following injection of thorium dioxide. Visualization of liver and spleen is possible after the injection of from 0.5 to 1 c.c. of thorotrast per kilogram of body weight, which dose is tolerated without evidence of immediate injury. The shape and position of the spleen undergo many variations and the authors feel these changes, under an artificial stimulus, should be interpreted with caution. The density after 493 days did not change.

The thorotrast is seen in the reticulo-endothelial cells of the liver, spleen, and bone marrow, and is scattered in fine granules throughout the liver cells. The early changes in the liver are hydropic degeneration, edema of the portal spaces, and dilatation of the periportal lymphatics. Later, there is usually recovery from the hydropic degeneration and a slight but definite increase in connective tissue. In the spleen, an early change simulating acute splenic tumor occurs, fol-

lowed later in the majority of cases by slight fibrosis. The bone marrow undergoes hyperplasia early, which is replaced eventually by exhaustion, manifesting itself by a partial disappearance of the blood-forming centers and serous atrophy of the fat.

The authors recommend, therefore, restriction of the intravenous injection of thorotrast for diagnostic purposes to incurable cases, until evidence is presented, based on studies in the human, demonstrating without doubt that the changes observed in the animals are not significant.

S. M. ATKINS, M.D.

COSMIC RAYS

Have Cosmic Rays Demonstrable Biologic Effects? R. B. Engelstad. *Strahlentherapie*, 1934, **51**, 672.

The author states that cosmic rays seem to have an inhibitory effect on growth or such biologic functions responsible for growth. On the other hand, his investigations showed that the absence of cosmic rays did not seem to have any serious effects on experimental animals (white mice).

ERNST A. POHLE, M.D., Ph.D.

DOSAGE

Advances in the Standardization of Practical Dosage in Roentgen and Radium Therapy. T. C. Neeff. *Strahlentherapie*, 1934, **51**, 650.

The author presents a series of curves and tables offering data which permit the computation of x-ray and radium doses in r.

ERNST A. POHLE, M.D., Ph.D.

EYE (THERAPY)

Roentgen Therapy of a Post-traumatic Cyst of the Iris. M. Lüdin and A. Bader. *Strahlentherapie*, 1934, **51**, 567.

The authors treated a case of cyst in the iris which had developed following an injury. Technic: 160 K.V., 4 mm. Al, 23 cm. F.S.D., 55 r per sitting. Six treatments were given over a period of five months. The cyst reduced in size and finally disappeared almost completely. The vision in the treated eye was good.

ERNST A. POHLE, M.D., Ph.D.

THE FOOT

Unilateral Periosteal Thickening of the Metatarsals. A. Zeitlin. *Röntgenpraxis*, November, 1934, **6**, 735-738.

Unilateral periosteal thickening of one or more metatarsals is not, by itself, a disease, but a sign of an abnormal condition of the foot which has led to anatomical changes and must be counted in the group of symptoms of "weak foot" described by Morton. This condition may be compensated for by adaptation of muscle and bone and may remain without symptoms. When the foot is used a great deal, symptoms of a "strained foot" are complained of. This unilateral periosteal thickening is not only of diagnostic, but also of prophylactic, importance.

HANS W. HEFKE, M.D.

FRACTURES

Ununited Intracapsular Fractures of the Femoral Neck Roentgenographically Considered. Arial W. George and Ralph D. Leonard. *Am. Jour. Roentgenol. and Rad. Ther.*, April, 1934, **31**, 433-441.

Statistics show that treatment of these fractures result in non-union or non-bony-union in 45 to 70 per cent. The apposition of the fragments is very important, owing to the absence of the periosteum. However, the blood supply is probably not greatly interfered with, since the ligamentum teres blood supply is adequate. The apposition of these fragments can be demonstrated by the "vertical view" with the use of the curved cassette. This view is stressed as being essential in every fracture of this type. Most of these fractures are of the leverage type and, therefore, impacted fractures are rare. It is felt that the vast majority of intracapsular fractures have not been properly reduced. The direct fractures are usually extracapsular or trochanteric and usually show coxa valga deformity, with little displacement, and a high percentage of bony union.

In a series of 20 consecutive intracapsular fractures, manipulations on the leverage theory resulted in over 70 per cent bony union. The maneuvers are, in their order, extension, adduction, internal rotation, and abduction. The study of old ununited fractures with the "vertical view" shows that absorption of the neck is uncommon, and, therefore, reveals possibilities in the chronic cases.

The authors feel that the large percentage of non-union or non-bony-union is due to lack of adequate apposition of the fragments and that the "vertical view" will result in better alignment. A greater percentage of cases of union are proven by their own series.

S. M. ATKINS, M.D.

GALL BLADDER (NORMAL AND PATHOLOGIC)

The Applied Physiology of the Extra-hepatic Biliary Tract. A. C. Ivy and G. S. Bergh. *Jour. Am. Med. Assn.*, Nov. 17, 1934, **103**, 1500-1504.

The gall bladder manifests, like the intestine, three types of activity: absorption, secretion, and motor activity. In the process of absorption, the gall bladder concentrates the hepatic bile that enters it from four to ten times. Chiefly water and certain inorganic constituents are absorbed. In the process of absorption the bile, which is alkaline as it leaves the liver, is slightly acidified. The bile renders the fats and cholesterol soluble at the acid reaction of gall-bladder bile. The acutely inflamed gall-bladder mucosa does not concentrate and does not evacuate. Cholesterosis of the gall bladder (strawberry gall bladder) is a condition characterized by lipid deposits in the mucosa of the organ. It does not interfere with the concentrating activity or emptying of the gall bladder unless associated with a moderate or severe cholecystitis.

The gall bladder secretes normally a mucoid fluid. When the gall bladder is acutely inflamed, a consider-

able quantity of limpid, sometimes blood-tinged, fluid is formed by the mucosa. The ducts secrete a colorless, slightly viscous substance, particularly when obstructed. Common duct obstruction for from twelve to fourteen days with a normal gall bladder in place produces green fluid in the ducts; with the gall bladder out or functionless, white fluid. "White bile" or lightly pigmented bile is found and can be produced experimentally under the following conditions: (a) common duct obstruction with a functionless gall bladder; (b) when the liver secretes against pressure in the presence of total obstruction; (c) toxic hepatitis (chloroform and the like); (d) high grade ascending infections or hematogenic hepatitis. In acute febrile diseases such as pneumonia, bile output is decreased, but a "white bile" is not secreted unless there is an associated hepatitis.

The motor activity of the gall bladder is of two types: first, rhythmic tonus changes, and second, a tonic contraction of the musculature of the gall bladder as a whole. The power of the normal gall bladder to contract is not greater than the secretory pressure of bile. The chief stimulus of gall-bladder contraction thus far discovered is the hormone cholecystokinin. The hormone may be extracted from the duodenal mucosa and, when injected intravenously, causes a more or less prolonged contraction of the gall bladder, with evacuation. The most effective excitants of hormone production are acids and fats, acting in the upper part of the intestine. All fats are effective, but egg yolk and cream appear to be the most active.

Whether or not the gall bladder will evacuate when stimulated depends on the tone of the sphincter of Oddi or duodenum, or the intramural resistance offered to the flow of bile from the common duct into the lumen of the duodenum. The sphincter of Oddi can resist up to 75 cm. of bile pressure, whereas the maximum expulsive pressure of the normal gall bladder is 30 centimeters. A spastic sphincter or duodenum can prevent gall-bladder evacuation. The sphincter of Oddi becomes incompetent soon after the removal of the gall bladder, showing that the gall bladder has some functional relation to the sphincter.

Prevention of gall-bladder disease may be aided by the daily evacuation of the viscus by appropriate intake of fat. Such prophylaxis should be a part of antepartum care. In acute biliary tract disease, foods which excite activity, such as fats, meats, and acid fruit juices, should be withheld. Magnesium sulphate or magnesium oxide, atropine or belladonna relax the sphincter. Bile salts only increase the fluid volume of the bile; they have a place in the therapy of chronic but not of acute biliary tract disease.

The evidence is inadequate to warrant the statement that actual damage is done the patient by removing a gall bladder that visualizes and empties. The fact, however, that physiologic and anatomic changes do result following the removal of such a gall bladder should deter the surgeon at least until medical control has been tried.

CHARLES G. SUTHERLAND, M.D.

Gallstones and Their Diagnosis in a Gall Bladder Not Filled by Dye. Emil A. Zimmer. *Röntgenpraxis*, November, 1934, 6, 723-727.

It is sometimes necessary to differentiate shadows caused by gallstones from kidney stones. When the gall bladder is functionless, other methods must be used. The gall bladder might be superimposed on the kidney shadow in antero-posterior roentgenograms. A semi-oblique exposure will bring the shadow of kidney stones closer to the spine, the shadow of gallstones farther away from it. A lateral examination might help if the density of the gallstones is sufficient. A gallstone shadow will be more clearly defined on a postero-anterior roentgenogram than on an antero-posterior one. By changing the position of the patient, the position of the stones in the gall bladder might change and the gall bladder itself changes its position, a fact which can be used in questionable cases to advantage.

HANS W. HEFKE, M.D.

GAS GANGRENE

The Importance of Roentgenologic Examination for the Diagnosis and Treatment of Gas Gangrene of an Extremity. Justus Schneider. *Röntgenpraxis*, August, 1934, 6, 522-524.

The gas formation in the soft tissues in cases of gas gangrene can be shown well in roentgenograms. A case is described in which roentgen examinations were used successfully to diagnose the disease, to localize the process, and to follow the clinical course of the disease. A recurrence was seen easily on re-examination and checked by surgical incision. It was possible to save the arm of the patient.

HANS W. HEFKE, M.D.

GASTRO-INTESTINAL TRACT (DIAGNOSIS)

The Unstable or Irritable Duodenum: Clinical Observations in 100 Cases. Julius Friedenwald and Maurice Feldman. *Jour. Am. Med. Assn.*, Dec. 29, 1934, 103, 2007-2011.

The term "unstable" is preferable, since at times a decreased rather than an increased irritability is noted. The underlying cause must be sought in an imbalance in the neuro-muscular apparatus of the duodenum, leading to a motor dysfunction and possibly also, to a certain degree of a secretory dysfunction without evidence of organic disease. Adhesive processes from chronic cholecystitis, adhesions between the duodenum and hepatic flexure, and those formed as a result of visceroptosis or following abdominal operations, or pressure on the duodenum from spinal deformities, ptosis of the right kidney or tumor of the pancreas or other abdominal organs, are mentioned as mechanical factors in etiology. Chemical causes are manifested in changes in the gastric secretion, regurgitation of bile and duodenal contents into the stomach due to absorption of toxic material from retained duodenal contents which cause disturbed motility in this portion of the bowel. Allergy has been observed as a definite etiologic factor in certain instances.

Derangement of the nervous system plays an important part in the production of this condition. It frequently arises in high-strung individuals, especially during periods of overwork and fatigue. It may be reflex in origin from chronic cholecystitis with or without pericholecystic adhesions, cholelithiasis, gastric ulcer, chronic appendicitis, and visceroptosis.

The superior portion of the duodenum, also known as the *cap* or *bulb*, is the most frequent site of the manifestation. The irritable bulb is characterized roentgenologically by the presence of (1) an increased motility with complete or incomplete emptying, (2) transient irregularities and fibrillation along the borders, (3) transient spastic manifestations, (4) tenderness and sensitiveness over the duodenum, and (5) absence of a definite ulcer filling defect. A series of illustrations diagrammatically outline tracings made from fluoroscopic observations.

Treatment is directed toward a restoration of this part of the bowel to normal tone, which is best accomplished by diet, rest, and improvement of the nervous system. All irritating foods and remedies should be omitted. Psychotherapy plays an important rôle in cases in which neurasthenic manifestations are prominent. In reflex causes, treatment must necessarily be directed to the primary disorder.

CHARLES G. SUTHERLAND, M.D.

Polyposis in the Entire Gastro-intestinal Tract. C. Gütig and A. Herzog. *Röntgenpraxis*, October, 1934, 6, 671-676.

A case of generalized polyposis in stomach, small intestine, and colon is described, in which the diagnosis was made during the life of the patient by means of roentgenologic examination. While the findings of the roentgen examination correspond with the autopsy as far as stomach and colon were concerned, only a few of the numerous polyps of the small intestines had been shown by the x-ray examination. The reason for it is that the increased and pathologic motility did not allow visualization of all the small intestinal loops. It is, furthermore, very difficult—often impossible—to get satisfactory demonstration of the mucosa relief of the small intestine. A stage preceding the formation of polyps in the small intestine is described which presents itself as an irregular formation of spurs on the ends of the transverse folds.

HANS W. HEFKE, M.D.

The Roentgen Diagnosis of Intermittent Ileus. R. Prévôt. *Röntgenpraxis*, October, 1934, 6, 655-663.

Roentgenologic examination of the small intestines seems, as yet, a more or less neglected field. Berg has pointed out that it is indicated quite often, even in acute diseases of the abdomen. An examination during an acute attack has to be done in as short a time as possible, and one must endeavor to make the diagnosis within an hour or two. The first step in such cases should be a fluoroscopic examination of the thorax (for pneumonia, infarct, pleurisy, and diseases of the heart); the behavior of the diaphragm should be watched

carefully for evidence of subphrenic processes. The next step is a flat film of the abdomen, after fluoroscopic observation of it, for the possible demonstration of gas-dilated loops of small intestine and gas under the diaphragm. Stones in the urinary tract and gall bladder must be looked for at the same time. A barium enema may be used in all cases of acute diseases of the abdomen, without danger. The administration of barium by mouth, however, might have disastrous consequences by making complete a hitherto incomplete obstruction. All these different methods of examination can be done within an hour.

Roentgenologic examination during an interval when a patient does not present any symptoms may be done much easier and more completely. Cholecystography and urography and complete examination of the gastrointestinal tract may be done. In the case of suspected intermittent small intestinal obstruction, it is of great importance to examine the small intestines at frequent intervals in order not to miss slight dilatation and temporary stoppage in the small intestine. Seven cases are described and the importance of such roentgenologic procedure and diagnosis is emphasized.

HANS W. HEFKE, M.D.

Proteins *versus* the Carbohydrates: An Inquiry into Their Gastric Digestion. Martin E. Rehfuess. *Jour. Am. Med. Assn.*, Nov. 24, 1934, 103, 1600-1603.

Direct investigation of the behavior of proteins and carbohydrates in the untraumatized normal stomach revealed that the gastric response in all varieties of foods is constant in type in the individual. One was found to be of a relatively slow type and another of a rapid type of gastric digestion. The secretory response could likewise be divided into groups, some showing a tendency to a low secretory output, others a presumed normal, and still others a hypersecretory type of response. In meat digestion alone an evacuation time of from two hours and thirty-five minutes to three hours and twenty-five minutes was noted in different types. The acid figures with meat were the highest of those encountered with any of the varieties of foodstuffs. The normal digestion of carbohydrates is attended by the maceration of the carbohydrate in an acid medium before it is available for further digestion in the bowel. Evacuation time is dependent on the articles ingested and the quantity of food. The average normal individual has a gastric digestion time somewhere near four hours and rarely exceeds five hours, during which no reasonable amount of fermentation can ensue. A falling off in secretion and a slight increase in the evacuation time is evidence of some functional inefficiency on the part of the chronic invalid.

A series of studies showed that even in diseased individuals of markedly different types there is no incompatibility between protein and carbohydrate digestion. There is no evidence either in the literature or in Rehfuess' investigation of such an incompatibility. It is manifest that the danger of such teaching is based on a lack of scientific evidence, and the unqualified acceptance of such a teaching can lead to the occurrence of

serious malnutrition as well as to a lighting up of tuberculosis and old infections.

CHARLES G. SUTHERLAND, M.D.

GENITO-URINARY TRACT (DIAGNOSIS)

Postpartum Pyelitis of Pregnancy: Treatment of Certain Cases without the Use of the Ureteral Catheter: Explanation Based on Physiology of the Bladder. D. K. Rose. *Am. Jour. Surg.*, September, 1934, **25**, 394-397.

In postpartum pyelonephritis, with bladder retention, in which catheter interference is indicated either from dysuria or toxicity, we meet with two entirely opposite types of bladder function. Either may exist separately or the two may co-exist to any degree.

The postpartum bladder showing a relatively fixed compensated bladder wall back of a physiologic block, motor and sensory, of the external sphincter, if of sufficient degree, requires continuous drainage when indicated by reason of infection. Such drainage primarily reduces bladder infection and, secondarily, urethral, pelvic, and kidney infection, by facilitating ureteral flow through a decompressed and perfectly drained bladder. Intermittent catheterization in such a bladder traumatizes in the presence of imperfect drainage and, therefore, tends to generalize or diffuse the infection. Irritative instillations in such bladders are contraindicated. Ureteral catheter drainage is indicated only when a primary ureteral block such as stone, stricture, etc., exists to complicate the usual clinical picture.

If sufficient degree of altered bladder function occurs, continuous bladder drainage is indicated until perfect function is restored.

The post-operative bladder with inhibited or functionally weakened bladder wall and with normal sphincter tone requires only intermittent catheterizations. Frequently, one to three will suffice to restore normal function. If not, the inhibition reflex is continued from the operative site. Irritating instillations in these bladders may be of value. Other post-operative types of retention are psychic or protective, permitting the bladder to over-distend.

DAVIS H. PARDOLL, M.D.

GRENZ RAYS

Biologic Experiments with Grenz Rays. F. Koch. *Strahlentherapie*, 1934, **51**, 541.

The author undertook extensive experiments with Grenz rays and studied the reactions on the skin, which he found cannot be used for dosage. Studies of the effect of Grenz rays on *lens esculenta* proved to be very suitable for a biologic dosimetry. The maximum dose determined in these experiments agreed well with clinical experience. The mitosis curve following the application of heavy doses of Grenz rays showed a different slope than the curves obtained following radium and x-ray exposure. It was interesting to note that the biologic effect of Grenz rays increased with decreasing wave length.

ERNST A. POHLE, M.D., Ph.D.

HEMOPHILIA

Bone and Joint Changes in Hemophilia. Leon Solis-Cohen and Samuel Levine. *Am. Jour. Roentgenol. and Rad. Ther.*, April, 1934, **31**, 487-491.

Hemophiliacs who reach the age of puberty often develop bone and joint lesions. Pathologically, there are three stages: First, hemorrhage into the joint, with thickening of the fibrous joint capsule; second, vacuolization in the epiphysis above the articulating surface, with the edges of the latter sharply etched and well defined, and opposing joint surfaces separated by a hemorrhagic effusion; third, the regressive phase; the loss by destruction or absorption of cartilage resulting in deformity and pseudo-lipping.

Roentgenologically, the diagnostic signs are as follows:

Acute or first stage.—Joint space widened and denser.

Second stage.—Thickening of the joint capsule and often a crater-like excavation in the extra-articular portion of the diaphysis. Shadows of an organized blood clot are found in the recesses of the joint and follow the outline of the joint capsule. The density of the synovial tissue may resemble the calcifications observed in myositis ossificans. Widened joint spaces occur without bony ankylosis. In the knee, the femoral condyles may be broadened.

Third or regressive stage.—The articular surfaces are irregular and the ends of the bones entering the joint may be deformed. Pseudo-osteophytes due to the hollowing out of the extra-articular surfaces of the articulating bones are observed. In the knee, the spine of the tibia is often deformed, and the intra-condylar notch widened. In the elbow, subperiosteal hemorrhage may undergo calcification. In the hip, the bone changes may resemble Perthes' disease. In the shoulder, the changes may simulate caries sicca.

S. M. ATKINS, M.D.

INFLAMMATORY DISEASES

Roentgen Therapy in Acute Inflammatory Diseases of the Mouth. R. K. Kruglikowa and S. N. Weissblatt. *Röntgenpraxis*, August, 1934, **6**, 527-530.

X-ray therapy is used extensively in many inflammatory diseases, but its use in inflammatory processes of the mouth and teeth has been neglected. The results in 103 cases are reported. In 66 patients with acute diffuse or localized osteomyelitis of the jaws, roentgen therapy alone led to a cure in 23, and improved the condition in the others so much that surgical procedures could be instituted much earlier than usual. In some very septic and almost hopeless cases this treatment led to improvement. Soft tissue phlegmons due to an osteomyelitis of the jaw responded well to x-ray therapy; the results appeared to be better than with the other conservative measures. Difficult eruption of the third molars, with infected pockets which caused considerable pain, was markedly improved by roentgen treatments, and the duration of the symptoms was much shortened as compared with the older methods. Neuralgias, after local anesthesia and surgical proce-

dures, were relieved in rather short time by irradiation. Acute lymphadenitis responded very quickly.

In 58 of the 103 cases of inflammatory diseases of the jaws and teeth, the results of roentgen therapy alone were good; in 45 cases the necessary surgery was made possible. There was quite often an acute aggravation of the inflammation from ten to twelve hours after irradiation. From one-eighth to one-twelfth of an erythema dose was given with 160 K.V., 4 ma., and a filter of 0.5 mm. of copper and 1 mm. of aluminum.

HANS W. HEFKE, M.D.

THE KIDNEYS

Treatment of Unilateral Urinary Fistulas by X-ray Destruction of the Kidney: A Clinical and Experimental Study. Nathan P. Sears. *Am. Jour. Obstet. and Gynec.*, September, 1934, **28**, 402.

The author reviews the literature concerning the effect of x-ray on the kidney, presents a case of urinary fistula cured by irradiation, and reports the result of his experimental work on the effect of irradiation on the kidney of the rabbit. In 1928, Klein successfully irradiated four patients with ureteral fistulas. This was followed by reports by Conrad, Halbfas-Ney, Soiland, and S  n  que, who were likewise successful in the irradiation of urinary fistulas.

The author's patient was a female, aged 49 years, who had suffered with hematuria, pain, and frequency for seven years. Roentgenographic examination revealed a shadow in the region of the left kidney. She subsequently developed fever, weakness, and a generalized rash, which was diagnosed as a toxic dermatitis. Cystoscopic examination revealed a left pyonephrosis. After several irrigations of the left kidney pelvis the rash disappeared and the patient's general condition improved. Following operation, a fistula developed which was treated by irradiation therapy. The anterior and posterior surfaces of the left kidney region were irradiated, employing the following factors: 156 K.V.P., 4 ma., 0.25 mm. Cu and 1 mm. Al filter, 20 in. distance, two and two-fifths E.D. divided equally between the two ports.

While the excretion of urine was noted to increase for a short period of time it later diminished in amount. Two months later she received a second series of similar x-ray treatments. Approximately six months later because some drainage from the wound persisted, surgical treatment of the fistula was performed. Since the operation failed to produce an improvement in the condition, the patient was again irradiated, and three E.D. were administered. The total irradiation at the surface was seven and four-fifths E.D. and the estimated dose at the kidney, four E.D. She was discharged perfectly well and has remained so.

In the author's experiments the right kidneys were removed from six healthy rabbits, and after a post-operative period of three months, the left kidneys were exposed at operation and irradiated. The factors employed were: 106 K.V.P., 4 ma., 10 in. distance, and 1 mm. aluminum filter. Two E.D. were given each rabbit at each exposure. Two animals received 2 E.D.,

two 4 E.D., and one, 6 E.D. The sixth animal died as a result of air embolism. Approximately four months later, autopsies were performed on the animals, the kidneys were removed and microscopic sections prepared. The kidneys which had received 2 E.D. showed, in scattered areas, evidence of varying stages of fibrosis and atrophy involving the glomeruli, with occlusion of the capsular spaces. There was also evidence of tubular destruction, with fibrosis and considerable round-cell infiltration. Sections of the kidneys which had received 4 E.D. showed a greater degree of involvement, with marked tubular destruction and subsequent partial regeneration and fibrosis. The glomeruli showed a fibrosis of the capsule, with some slight hyaline change. The surviving convoluted tubules showed varying degrees of degenerative change. There was a diffuse round-cell infiltration. In those kidneys which had received 6 E.D. there was marked tubular destruction, with subsequent fibrosis. The surviving tubular epithelium showed the same degenerative changes as in the other sections, with scattered areas of apparent compensatory hypertrophy. There was rather diffuse hyaline degeneration of the interstitial tissue, with comparatively slight round-cell infiltration.

The author concludes that it is possible with modern x-ray therapy to destroy normal and diseased kidneys. In general, the epithelial structure of the kidney is replaced by connective tissue as the result of irradiation. The vascular and glomerular units are the last to be affected. The importance of carefully determining the exact location of the kidney so that it will receive all the rays intended for it is stressed by the author.

J. N. AN  , M.D.

KNEE JOINT

Pneumoradiograms of the Knee Joint. J. Oberholzer. *R  ntgenpraxis*, October, 1934, **6**, 646-652.

The method of Bircher has become an important diagnostic means to demonstrate the knee joint. It is a combination method inasmuch as neo-skiodan is introduced with oxygen. The neo-skiodan causes a thin shadow on the wall of the capsule, the menisci, the cruciate ligaments, and the cartilage. The oxygen causes a negative contrast, and the different parts of the knee joint cavity are nicely demonstrated in this way. Several cases are described and many roentgenograms are reproduced to prove the diagnostic value of the procedure. Strictly aseptic and correct technic is necessary for pneumoradiograms. This special technic allows a much more exact diagnosis of the knee joint than does the plain roentgenogram, especially in pathologic conditions of the joint capsule, ligaments, menisci, and cartilage.

HANS W. HEFKE, M.D.

THE LUNGS

Lung Abscess. Harold Brunn. *Jour. Am. Med. Assn.*, Dec. 29, 1934, **103**, 1999-2003.

The scope of this paper is limited to that type which has its beginning as an acute putrid abscess—foul

smelling, containing elastic tissue, usually aspiratory in origin, and containing a multiplicity of bacteria, both anaërobic and aërobic; excluding bronchiectasis, abscesses on a carcinoma basis, and those produced by foreign bodies. Under the term of "medical treatment" the author has included inhalations, postural drainage, bronchoscopy, artificial pneumothorax, phrenicectomy, arsphenamine, and the application of roentgen therapy. Surgical treatment includes only open drainage and lobectomy. The advantages of postural drainage are not nearly so great in abscess as in bronchiectasis. It is valueless until an abscess has broken into a bronchus. To apply this remedy to a very sick patient—cyanotic, with high fever, rapid pulse, and a low vital capacity—is to court disaster. Pulmonary ventilation is facilitated in the upright position; vital capacity is generally higher, and the volume of the lung is greater, the accessory muscles of respiration can be used to better advantage, and the diaphragm is lower than in the recumbent position. Intrapleural pressure has been found less negative in the recumbent than in the upright position. A less negative intrapleural pressure will limit pulmonary ventilation and interfere with pulmonary circulation. All these factors work an even greater disadvantage in the position of postural drainage—produce compression and atelectasis of the lung and so lower its resistance that infection may take place, with intrapulmonary spread.

Bronchoscopy is useful for the purpose of eliminating the possibility of a foreign body, for the diagnosis of a malignant condition or stenosis as a cause of the abscess, and for the purpose of shrinking granulations to permit of better drainage through the bronchus, but the procedure cannot be carried out with sufficient frequency on a sick patient to really keep an abscess drained surgically. It is not entirely devoid of the danger of setting up further inflammation.

Artificial pneumothorax, in the author's experience, has risks that do not justify its use. It is applicable to but few, it tends to break down adhesions, and not infrequently causes rupture into the pleural cavity, with formation of a putrid empyema, and entails delay just when surgery would be beneficial.

Temporary phrenic paralysis is best applied for abscess of the lower lobe with adhesions to the diaphragm but has very limited application. Arsphenamine as a cure has been unsatisfactory in Brunn's experience.

Roentgen therapy, to cause more rapid liquefaction of the abscess, early rupture into a bronchus, clearing up of surrounding pneumonitis, and delimitation of the disease is probably advantageous and may prove a most valuable adjuvant, but experience does not yet warrant a definite conclusion as to its value.

Roentgenograms should be taken in various planes and with varying densities and should be used frequently to follow the course of the disease. They should not be relied on absolutely: in some cases the clinical course offers a better basis of judgment. The use of iodized oil seldom gives any information in lung abscess.

Surgery offers definite advantages in the treatment of lung abscess. Perfect drainage of the abscess cavity can be obtained, leaving no undrained pockets from which extension can take place. Through-and-through aëration of the cavity and bronchi results. By a liberal removal of the roof of the cavity, its early collapse is facilitated. Certain important requisites are mentioned: (1) careful localization; (2) the performance of the operation in two or even more stages; (3) the use of the cautery or diathermy knife in exposing the abscess, and (4) the use of compression by a gauze pack or paraffin.

A study of charts and tables based on medical and surgical treatment shows definitely the advantages of positive action in the treatment of lung abscess.

CHARLES G. SUTHERLAND, M.D.

Serial Bronchography for the Diagnosis of Purulent Diseases of the Lungs. Pedro L. Farinas. *Röntgenpraxis*, September, 1934, 6, 569-582.

The changes of the bronchial tree in lung abscess depend on the stage of development of the process. In the pre-expulsive phase of the acute period, the bronchographic picture is normal, but alveolar dispersion is missing because the 40 per cent iodipin cannot fill the alveoli which are already filled by exudate.

The bronchographic appearance is different in the phase of abscess formation. The cavity usually does not fill. The bronchial tree may look normal, even though the alveolar dispersion is absent, or there may be a cylindrical or pearl-string-like dilatation of the draining bronchus.

If one is not dealing with a basal abscess, the bronchi of the base may also be dilated, which may be explained by the fact that the secretion of the cavity drops into the basal bronchi, continuously reinfecting them in this way. In one type of acute abscess, the pathologic changes are found simultaneously in the parenchyma and in the bronchi, which dilate prematurely and present the picture of cylindrical dilatation.

During the chronic stage the abscess cavity usually may be filled by the contrast material, and the surrounding bronchi show saccular dilatation. The draining bronchi show either cylindrical or pearl-string-like dilatation and the basal bronchi also may show this type of bronchiectasis.

If the cavity is not visible, it is difficult and sometimes impossible to differentiate between massive bronchiectasis and an abscess leading to a bronchiectasis. Occasionally one can find in the bronchogram an abscess cavity of fair size and, surrounding it, several smaller cavities of saccular appearance which are to be explained by bronchiectatic dilatation.

HANS W. HEFKE, M.D.

Round Shadows in the Lungs. Ladislaus Udvary. *Röntgenpraxis*, November, 1934, 6, 713-723.

Round, well-circumscribed shadows in lung roentgenograms are considered usually as typical for tumors; in publications of the last few years, however, many other causes have been described.

Primary carcinoma of the lung or bronchial carcinoma in the hilar regions may cause the x-ray appearance of a well-circumscribed round shadow when seen at an early stage; usually, however, such a tumor shows irregular lymphangitic extension or causes symptoms of atelectasis and secondary infection. Almost all metastatic lung tumors show the round type of shadow, especially the sarcomas. Benign tumors—for instance, dermoids—may present the same picture as malignant tumors. Echinococcus cysts cause the roentgen appearance of single or multiple round shadows; only the clinical symptoms and sometimes the Escudero-Nemenow symptom of change of the shape of the shadow in inspiration and expiration must decide the diagnosis.

Actinomycosis and syphilis are known to have shown regular round areas of infiltration in the lungs.

Tuberculosis of the lungs occasionally may make considerable difficulties in differentiating it, roentgenologically, from tumors, when it appears in well-circumscribed round or oval shape in roentgenograms. The infiltrations may be even multiple. Roentgenologic follow-up and other clinical symptoms must help to make the diagnosis.

Round shadows have been seen as the expression of bronchopneumonia, even multiple. Especially the influenza-pneumonias seem to show this atypical appearance. Three cases of puerperal septic pneumonias have been seen to cause round, fairly circumscribed areas of density in roentgenograms of the lungs.

It becomes more and more evident that the well-defined round shadows seen in lung roentgenograms are by no means always caused by malignant tumors; one must consider many other diseases, and history and clinical examination are often necessary for a correct diagnosis.

HANS W. HEFKE, M.D.

The Bronchopulmonary Segment, with Special Reference to Putrid Lung Abscess. Ameil Glass. *Am. Jour. Roentgenol. and Rad. Ther.*, March, 1934, **31**, 328-332.

Clinical, operative, and autopsy studies at Mt. Sinai Hospital (New York) have demonstrated that putrid lung abscess in its primary evolution involves definite and circumscribed regions of the lungs. These are subdivisions of lobes and possess constantly a definite size, shape, and position. These have been designated bronchopulmonary segments and act as the unit of localization in lung abscess. Each is named according to the position in the thoracic cage and pulmonary architecture.

On the postero-anterior view, roentgenologically, abscess in the inner lung-field represents disease of the posterior segments; lateral field, of the axillary segments, and middle field, either anterior or posterior, and a lateral view is necessary. The exception is the abscess adjacent to the heart and situated on the diaphragmatic dome; this lies in the mesial segment.

S. M. ATKINS, M.D.

THE MASTOIDS

The Roentgenologic Diagnosis of Mastoiditis. Leonard Kraus. *Röntgenpraxis*, August, 1934, **6**, 497-508.

A roentgenogram of the mastoids is necessary for a complete examination of the ears. The author reports his findings in a special group of mastoid cells, which he calls "hypolabyrinthine cells." Anatomically they are situated below the antrum toward the tip of the mastoid and just below the horizontal and posterior semicircular canal, extending toward the medial end of the petrous bone. Because they are in close proximity to the sigmoid sinus and the seventh nerve they may lead to serious complications if they are not recognized and opened by the surgeon. The clinical symptoms of involvement of this cell group are dull unilateral headache and vertigo, sometimes without tenderness over the mastoid. These cells are occasionally the only ones involved while all other cells remain normal. Often there are other abscesses, usually in the tip. The hypolabyrinthine cells can almost always be found on roentgenograms, when the other cells are well developed. The absence of aeration of these cells as compared with the normal side indicates pathology. A roentgenologic examination of the mastoids is not complete without paying attention to this group of cells, and findings in them might be of great importance to the surgeon.

HANS W. HEFKE, M.D.

PEPTIC ULCER (DIAGNOSIS)

Complications of Peptic Ulcer: Their Prognostic Significance. Sara M. Jordan and Everett D. Kiefer. *Jour. Am. Med. Assn.*, Dec. 29, 1934, **103**, 2004, 2005.

Successful management, the purpose of which is to produce a remission and prevent a recurrence, must be the thought, rather than cure, in handling this disease. This depends on various intrinsic and extrinsic factors. Such well-known factors as limitation of nervous tension and fatigue and adherence to a careful regimen of living are at least relatively within the control of the patient and the physician. The intrinsic factors comprise (1) the nature of peptic ulcer in general and (2) the nature of the individual ulcer, particularly its location, size, and complications. The complications considered in the authors' study are pyloric obstruction, hemorrhage, and intolerance to alkaline therapy. Of 79 cases, only 11 per cent required surgery for the immediate relief of obstruction. Relief was obtained in 89 per cent by hospital management of from one to three weeks' duration. In 34 per cent of patients relieved by medical management there were recurrences—in nine obstruction and in fifteen distress alone or with hemorrhage. The tendency to recurrence in a given group was just as great at the end of five years as it was during the previous years. In a group of 42 patients giving a history of one gross hemorrhage, 17 per cent had recurrence during the first year; during the first five years, 43 per cent experienced a recurrence, and 57 per cent had an uninterrupted remission. The his-

tory of two or more gross hemorrhages was decidedly more serious. In a group of 19 patients, only 21 per cent remained free from recurrence for five years. In another group of 13 cases, 54 per cent had recurrence in a two-year period. The prognosis of patients with multiple hemorrhages appeared to be definitely bad.

Alkalosis from alkali medication was a complication of therapy arising when efforts were made to neutralize the stomach contents with sodium bicarbonate. In nearly all cases the condition was mild and transient and easily relieved by adjusting the dose. Severe alkalosis indicated a particularly severe lesion and a marked disturbance in gastric secretion, as well as renal disease: 70 per cent had a recurrence within two years.

CHARLES G. SUTHERLAND, M.D.

PLEURISY, MEDIASTINAL

Mediastinal Pleurisy. Ladislaus Udvardy. *Röntgenpraxis*, September, 1934, 6, 585-593.

Comparatively little has been written about mediastinal pleurisy and yet the clinical and roentgenologic appearance of it is very definite. Tuberculosis is the most common etiologic cause, probably due to the caseation of mediastinal glands. In such cases the hilus itself is dense, and one sees a shadow of increased density beside the mediastinum, wider in the upper portions. If one makes a radiogram of a chest in Fleischner's position (lordosis of the lumbar spine), one may see a much larger, more intensive, usually triangular shadow which represents the thickened pulmonary and mediastinal pleura, and the thickened interlobar space filled by exudate.

Tumors, especially of the hilus glands, lung abscesses, and abscesses originating in the vertebrae also may be causative agents.

Of more importance and more interest are cases in which simple pleurisy is the etiologic factor. Clinical history in such cases is often indefinite. The patient complains of pleural pain, high fever, and severe cough, the latter often spasmodic. Such mediastinal exudates have a triangular shape, with the base toward the lower portions. Again Fleischner's position is of help.

Mediastinal pleurisy in the inferior mediastinum is much harder to diagnose, and roentgen examination alone is not sufficient usually for diagnosis. Several such cases are described, and it is pointed out that a pericardial effusion easily may be mistaken for it. Fluoroscopic examination seems to be much more important for mediastinal pleurisy than films. If films are taken, they are best taken with the Bucky diaphragm.

HANS W. HEFKE, M.D.

THE PROSTATE

A Case of Sarcoma of the Prostate Cured by Roentgen Therapy. L. Popp. *Röntgenpraxis*, October, 1934, 6, 680, 681.

Early carcinoma of the prostate gland should be operated on. Post-operative irradiation with large fields

and high voltage should be used on account of the frequency of early metastasis. In inoperable cases, the trial of roentgen or radium therapy is permissible, but the results are not encouraging. Pain caused by bone metastasis often may be relieved by x-ray therapy.

Sarcomas of the prostate gland are seen much less frequently. Histologically, they are lympho- or adenosarcomas. The treatment should be surgical removal and post-operative radiation. Lymphosarcomas are so radiosensitive that roentgen therapy alone is sufficient. The case is reported of a 24-year-old man who had an inoperable sarcoma of the prostate. After repeated series of x-ray treatment, the tumor disappeared and the patient was well two years after the treatments.

HANS W. HEFKE, M.D.

RADIATION EFFECTS

The Fibrinogen Content of the Blood under the Influence of Roentgen Irradiation and the Primary Effect of Radiation. A. Held and H. Hülbach. *Strahlentherapie*, 1934, 51, 664.

It has been known that the coagulation time of the blood has decreased following exposure to roentgen rays. The authors found in their experiments that this is probably due to an increase of the fibrinogen. The reticulo-endothelial system is undoubtedly involved in the reaction. The drop in the fibrinogen content of the blood which follows immediately after the exposure to roentgen rays is explained as a direct effect of radiation.

ERNST A. POHLE, M.D., Ph.D.

Epilation of Rabbit Skin following Irradiation. G. H. Klöveborn. *Strahlentherapie*, 1934, 51, 689.

The author studied the epilation in the skin of rabbits following exposure to roentgen rays. He comes to the conclusion that rabbit skin is not a suitable object for biologic studies of epilation. He found that it occurs in the rabbit between 840 and 2,100 r, anywhere from 18 to 35 days following exposure. He also briefly reports the histologic changes found in the skin following irradiation.

ERNST A. POHLE, M.D., Ph.D.

RADIUM

Radium Therapy in Malignant Tumors of the Upper Respiratory Tract: Results Based on Five Years' Observations. A. Lång. *Strahlentherapie*, 1934, 51, 573.

The author presents an analysis of 59 cases with malignant tumors in the nose, epi-, meso-, and hypopharynx. They were treated by x-rays and radium, either alone or combined. The results are compiled in seven tables and should be studied in the original. The author removes the lymph glands if there is no evidence of involvement; all others are subjected to irradiation.

ERNST A. POHLE, M.D., Ph.D.

ROENTGEN SICKNESS

"Peremesin" for the Prevention of X-ray Sickness. Hermann Kuhn. *Röntgenpraxis*, September, 1934, 6, 615, 616.

"Peremesin" (Heyden), a colloidal cerium preparation, which is claimed to be non-toxic and harmless, was used by the author in 60 cases for the prevention of x-ray sickness. While, previously, many patients complained of sickness, such complaints have not been heard since administering the drug. Two tablets were taken before, and four tablets in intervals after, the irradiation.

HANS W. HEFKE, M.D.

THE STOMACH

Multiple Diverticula in the Cardiac End of the Stomach. Kurt Kremser. *Röntgenpraxis*, August, 1934, 6, 524-527.

A single diverticulum of the stomach has been reported, but is rare. In the patient seen by the author, four small diverticula were demonstrated in the cardiac end of the stomach. The barium remained in one of them for three hours. The author believes that the diverticula were congenital.

HANS W. HEFKE, M.D.

The Diagnosis of Lymphosarcoma of the Stomach. O. Spitzenberger. *Röntgenpraxis*, October, 1934, 6, 667-670.

Lymphosarcomas of the stomach are relatively rare tumors and usually the roentgenologic diagnosis is impossible to make. There seem to be a few facts which might point to lymphosarcoma, considering differential diagnosis from carcinoma: first, its localization on the greater curvature side of the fundus; second, the involvement of the diaphragm by direct extension, and furthermore, clinically, the very marked loss of weight in a very short time, and the severe gastric pain. This differentiation is of some importance because lymphosarcomas may be benefited by roentgen therapy. One case is described in which a large lymphosarcoma of the fundus was diagnosed roentgenologically, was treated by x-rays, and received much benefit by these treatments.

HANS W. HEFKE, M.D.

Benign Tumors of the Stomach. Martin Simonsen. *Röntgenpraxis*, October, 1934, 6, 663-666.

The roentgenologic characteristics of benign tumors of the stomach are well known (smooth borders, round or oval filling defects, mobility of the tumor by the palpating hand, absence of changes in the mucosa surrounding the defects, undisturbed paristalsis). Three cases are reported: first, a fairly movable benign tumor of the pylorus; second, an adenomatous polyp on the greater curvature, which was found to show early malignant changes at autopsy, and third, a malignant polyp of the antrum which could have been mistaken for a benign tumor. It is pointed out that the question of the benign or malignant nature of a circumscribed gastric tumor cannot be determined by roentgen examination alone. Other clinical symptoms, especially the sedimentation time, must be considered, and even then a correct diagnosis can be made, frequently, only by microscopic examination of the tissue after surgical removal.

HANS W. HEFKE, M.D.

TUBERCULOSIS, INTESTINAL

Intestinal Tuberculosis: Pathologic and Roentgenologic Observations. Russell L. Boles and Jacob Gershon-Cohen. *Jour. Am. Med. Assn.*, Dec. 15, 1934, 103, 1841-1845.

Clinically, the diagnosis is seldom made with any degree of certainty although it is presumed to exist in many cases. Numerous pathologic studies show a consistently high incidence of intestinal tuberculosis associated with pulmonary tuberculosis, the incidence varying from 50 to 90 per cent. Analysis of autopsies studied was undertaken in order to determine (1) if tuberculosis of the intestine, whether hyperplastic or ulcerative, occurred more frequently than is suspected in the absence of pulmonary tuberculosis; (2) its incidence and relation to the type of pulmonary tuberculosis, and (3) the incidence of associated tuberculous disease of other abdominal viscera.

Of 1,000 autopsies studied, tuberculosis of the lungs was found in 226 cases (23 per cent). No evidence of it was found in 774 cases. In the entire 774 negative pulmonary cases no evidence of tuberculosis of the intestine, either hyperplastic or ulcerative, was found. In the 226 cases of healed and active pulmonary tuberculosis, an ulcerative type of intestinal lesion occurred in 63 (28 per cent). Primary hyperplastic tuberculosis or tuberculoma of the large bowel was not observed in the 1,000 autopsies, and it must be regarded, therefore, as a most infrequent variety of intestinal tuberculosis in adults. It may be more common in children, very few of whom were included in this study.

Of the 226 cases of pulmonary tuberculosis, the type and incidence of lung lesions were as follows: fibro-ulcerative cavernous, 105 cases (46 per cent); chronic fibroid, 85 (38 per cent); exudative, 22 (10 per cent); miliary, 12 (5 per cent), and tuberculous pneumonia, 2 (1 per cent).

Intestinal ulceration does not occur in the healed fibroid cases. The highest incidence of intestinal ulceration was observed in the fibro-ulcerative cavernous type, the next highest in the exudative pulmonary lesion. In 12 miliary cases of pulmonary tuberculosis, intestinal ulceration was not seen in a single case; a miliary lesion of the serosa was not infrequently noted. The authors' findings would appear to support the contention that intestinal mucosal lesions are caused by swallowed tubercle bacilli or enterogenous infection and that intestinal serosal lesions are probably due to blood-borne tubercle bacilli or hematogenous infection. Primary hyperplastic tuberculosis or tuberculoma of the bowel rarely occurs, whereas carcinoma, which it may simulate, is not unusual in the tuberculous subject.

As an important aid in the diagnosis of ileocecal tuberculosis, the authors recommend the double contrast enema. It reveals the indirect signs as segmental irritability and hypermotility and, in addition, provides an accurate demonstration of the actual morbid anatomic changes of the diseased segments of the bowel.

CHARLES G. SUTHERLAND, M.D.

TUBERCULOSIS, PULMONARY

The Effect of Initial Tuberculous Infection on Subsequent Tuberculous Lesions. J. Arthur Myers and Francis E. Harrington. Jour. Am. Med. Assn., Nov. 17, 1934, 103, 1530-1535.

Tuberculous lesions which develop in tissues that are not sensitive to tuberculo-protein are designated as primary lesions, first infection type of lesions, or, if in the lung, childhood type of tuberculosis. The diagnosis of the first infection type of tuberculosis is made primarily by the tuberculin test. The roentgenogram plays a minor rôle, while symptoms and physical signs are of little value. The reinfection type of tuberculosis develops on tissue that is sensitive to tuberculo-protein. In nature, so far as is known, such sensitiveness is produced in the human tissues only by a first infection type of tuberculosis. Reinfection foci may be divided into two groups, acute and chronic. The best examples of acute reinfection types are miliary disease and diffuse meningitis. Good examples of the chronic form of reinfection type of tuberculosis are disease of the bones, joints, and lungs. Here the roentgenogram is the most valuable diagnostic agent. Although this type of tuberculosis may be present in the lung a long time before it is sufficiently large to cast a shadow on the x-ray film, it will be detected by this method of examination earlier than by any other.

The authors do not make roentgenograms of the chest in children under ten years of age, even of the children who react positively, unless there is some special indication. The cost is too great to justify the small findings. The period of greatest danger, during which roentgenograms should be made periodically, begins about the age of ten or eleven years. After that age roentgenograms should be made periodically of the chests of all positive reactors.

CHARLES G. SUTHERLAND, M.D.

Bronchography, an Essential and Safe Adjunct in the Study of Pulmonary Tuberculosis. J. E. Murphy. Am. Jour. Roentgenol. and Rad. Ther., March, 1934, 31, 301-307.

Bronchography is essential in the following:

1. Interpretation of pathology of tuberculosis—(a) demonstration of bronchiectasis which so frequently accompanies it—60 per cent of 65 cases; (b) solution of baffling areas into clear pathology.

2. In the differentiation of parenchymal cavities from bronchial dilatation, and in cases in which selective collapse is to be practised, it localizes both the lobe and cavity.

3. Clinical explanation of a productive cough with negative sputum.

The limitations are:

(1) The solution may not enter into a cavity due to disease and secretions.

(2) Slight dilatation may be due only to the inspiratory phase and may be normal in the expiratory phase.

The contra-indications are:

1. Acute tuberculosis accompanied by fever;
2. Debility;
3. Recent hemorrhage, in which case it is best to wait ten days.

Technic.—The intratracheal route is employed, with the catheter introduced intranasally, under local anesthesia. Injection is made with roentgenoscopic control.

Numerous films are shown illustrating the conditions. S. M. ATKINS, M.D.

Bronchography in Relation to the Pathology of Pulmonary Tuberculosis. B. P. Potter. Am. Jour. Roentgenol. and Rad. Ther., March, 1934, 31, 308-318.

The following problems of pathology are clarified:

1. Bronchiectasis in tuberculosis is demonstrated in a high percentage in the chronic fibro-ulcerative lesions.
2. Annular shadows are differentiated into cavities, pleural pockets, encapsulated pneumothoraces, and emphysematous blebs.
3. Localization of the pathology in the particular lobe or lobes involved is accomplished.
4. Differentiation between pleural and parenchymal pathology is made, especially when the lung is obscured by pleural changes.
5. Differentiation between densities cast by un-aerated lung and similar densities due to other causes is established.

Numerous films are shown illustrating the conditions. S. M. ATKINS, M.D.

Round Foci Type of Pulmonary Tuberculosis. Samuel Bruck. Am. Jour. Roentgenol. and Rad. Ther., March, 1934, 31, 319-322.

A case is cited wherein a few sharply circumscribed shadows resembling metastatic malignancy were seen in the lungs and which were proven to be tuberculosis. These by themselves, as proven by similar cases reported (but few in the literature), present usually no clinical symptoms and usually do not break down or disappear, although in the case reported these did happen. They may or may not be accompanied by the usual roentgen manifestations of tuberculosis.

Pathologically, the lesions appear as rounded parenchymatous consolidations surrounded by a capsule of fibrous tissue without any surrounding tissue reaction. They are not primary lesions of tuberculosis, in that there is no accompanying adenopathy and so few of these cases are seen. This type of tuberculosis is to be kept in mind when findings resembling metastatic malignancy are seen in the lungs, but in which no primary lesion can be demonstrated.

S. M. ATKINS, M.D.

Hematogenous (Non-miliary) Pulmonary Tuberculosis. Max Pinner. Am. Jour. Roentgenol. and Rad. Ther., April, 1934, 31, 442-457.

This is a report based on 28 cases, 14 of which came to autopsy. Roentgenologically, the disease starts

with multiple small foci, usually symmetrically distributed throughout both lungs. The reasons for assuming a hematogenous spread are: (1) Even distribution of the lesions; (2) frequent absence of older pulmonary foci; (3) frequent association of extra-pulmonary lesions.

Röntgenologic Characteristics.—Early lesions appear as scattered fluffy areas of increased density with blurred borders, fairly homogeneous, and varying in size. The distribution may be almost as regular and dense as in acute miliary tuberculosis, or the lesions may be confined to the upper thirds of the lungs, especially in children. In the early stage, it occurs in two different aspects. (1) Small, fairly evenly distributed foci of slight density are seen, up to two or three millimeters in diameter. Individual foci, in contradistinction to miliary tuberculosis, show soft stringy lines between the more globular shadows. (2) The single lesions, about one to two centimeters in diameter, have borders ill-defined. Both types usually show enlargement and possible caseation of hilar lymph nodes. Most frequently the upper third or half of both lungs is affected.

The further roentgenologic development of these foci occurs along varying but characteristic lines. There may be complete resorption or calcification. The latter is usually initiated by soft circumfocal shadows. Differing from true primary foci, calcification occurs only in this type of tuberculosis. Another characteristic is, in addition to the calcification, that the stringy elements become a thin but dense network of sharp lines. Another development is bronchogenic phthisis. The clinical course differs from bronchogenic tuberculosis in that frequently there is total absence of symptoms. There is very little sputum and only rarely is sputum positive. Pathologically, the major part of the involvement is in the interstitial tissue.

S. M. ATKINS, M.D.

TUMORS (DIAGNOSIS)

Roentgen Diagnosis of Mediastinal Tumors and Their Differentiation. George E. Pfahler. *Am. Jour. Roentgenol. and Rad. Ther.*, April, 1934, **31**, 458-469.

This is a study based upon a review of 219 cases diagnosed as tumors. In their study, a number of factors must be determined: (1) size; (2) shape; (3) location; (4) relation; (5) pulsation; (6) movement. All methods of radiologic examination must be employed, if necessary.

Substernal thyroid, enlarged thymus, dermoid cysts, diverticulum of the pericardium, lipoma, fibroma, neuroma, aneurysm, lymphosarcoma, Hodgkin's disease, leukemic lymphoma, leukosarcomatosis, primary carcinoma, metastatic carcinoma, tuberculous lymphoma, syphilis, actinomycosis, and mycosis fungoides are thoroughly reviewed and illustrative cases cited.

S. M. ATKINS, M.D.

TUMORS (THERAPY)

Roentgen Therapy of Bone Sarcoma. K. Goldhamer. *Strahlentherapie*, 1934, **51**, 636.

The author reports a case of a man, 53 years of age, who on roentgen examination showed a large-sized tumor in the right humerus. Because of the destructive nature of the process the diagnosis of a sarcoma was made. Heavy doses of roentgen rays were applied over a period of two years; the tumor responded well and roentgenograms are shown in the article taken at certain intervals during that period. The author feels that the tumor is in all probability a round-cell sarcoma. No biopsy.

ERNST A. POHLE, M.D., Ph.D.

Studies in the Diagnosis and Treatment of Teratoma Testis. Russell S. Ferguson. *Am. Jour. Roentgenol. and Rad. Ther.*, March, 1934, **31**, 356-365.

The diagnosis of this condition is rarely made. Only 11 cases among 124 seen at the Memorial Hospital (New York) were free from local recurrence or metastasis, although 20 per cent of these patients sought medical advice within the first six months of the disease. This tumor constitutes 2.09 per cent of all malignant tumors in males and 3.39 per cent of all genito-urinary tumors.

There are no distinctive clinical features; even therapeutic test of radiation fails. It is best to delay operation until the diagnosis is accurately established. Of 59 new admissions from October, 1930, to October, 1932, the diagnosis was verified by histologic examinations in every case. All have had quantitative study of Prolan A in the urine.

This paper is a study of the relation of the biologic behavior of this tumor to radiosensitivity and to the pathologic anatomy of the disease, as well as the efficacy of different types of treatment. It is shown that the best results are from the study of the biologic behavior before, during, and after irradiation.

Relation of Radiosensitivity to Excretion of Prolan A.—Of 13 patients having tumors of the radioresistant type following irradiation, five are alive without disease from one to three years, and eight dead. In those who died, there was no decrease or only temporary decrease of Prolan A. In those alive, Prolan A dropped sharply. Of 22 patients having tumors of the radiosensitive type, thirteen are alive one to three years, and nine dead. In those alive, Prolan A dropped promptly to below 400 mouse units per liter of urine within two weeks after the termination of irradiation. With recurrence, the Prolan A increased and was lowered again by irradiation. Those patients who died showed no decrease in the Prolan A.

Prognosis based on histologic structure was not dependable, for about 50 per cent of the radioresistant survived and about 50 per cent of the radiosensitive succumbed. Pathogenesis and pathologic anatomy as basis for selection of therapy show the rationale of radical surgery to be entirely discredited. Only 6 per cent of teratoma testis tumors are of the adult type. These run a prolonged clinical course and metastasis is late. Embryonal carcinoma is active and metastasizes rapidly to lumbar, epigastric, mediastinal, and cervical lymph nodes and to the lungs.

Treatment.—That there is no justification for either simple orchectomy or radical operation is shown by the most recent statistics of Hinman or review of Wasterlain, on the basis of clinical results at the end of five years.

Irradiation.—In 154 cases (at Memorial Hospital), Dean reports 29.2 per cent alive and without evidence of disease at the end of five years, of which 74.6 per cent were inoperable on admission. Of 100 patients who had radical operation, as reported by Hinman, 17 are alive and without evidence of disease after five years. Irradiation results have improved since the quantitative study of Prolan A in the urine, for by this means, recurrence is easily detected.

S. M. ATKINS, M.D.

THE UTERUS

The Treatment of Erosions of the Uterus with Roentgen and Radium Rays. A. J. Kuratschenkow. *Strahlentherapie*, 1934, **51**, 622.

Since the erosion of the cervix is often a forerunner of carcinoma, adequate treatment should be instituted in the early stages. Good results have been obtained by both radium and x-ray treatment: 480 to 2,000 mg.-hr. usually suffice. Roentgen technic: 110 K.V., 3 mm. Al, 75 r, or 165 K.V., 0.5 Zn + 3 Al, 250 r. If the lesion responds, it results in a solid scar which usually does not develop a recurrence, and there seems to be no danger of malignant degeneration.

ERNST A. POHLE, M.D., Ph.D.

Results in the Treatment of Carcinoma of the Cervix by the Women's Clinic of the University of Breslau. W. Reiprich. *Strahlentherapie*, 1934, **51**, 601.

The author analyzes the statistics, giving the results obtained in the surgical and radiological treatment of carcinoma of the uterus seen in his own clinic. Radiation therapy consists usually of a combined x-ray and radium treatment. The total radium dose in the average case is 5,000 milligram-hours. In roentgen therapy the customary deep therapy technic is used with one anterior, two posterior, and one perineal field. The total dose effective at the site of the disease amounts to from 110 to 120 per cent H.E.D. Tables are also given permitting a comparison with the results obtained by other leading clinics. The author comes to the conclusion that the best results are to be expected in operable cases from a combination of surgery and irradiation.

ERNST A. POHLE, M.D., Ph.D.

THE WRIST

Hereditary Synostoses of the Small Bones of the Hand and Foot: Hereditary *os tibiale externum*. Jürgen Mestern. *Röntgenpraxis*, September, 1934, **6**, 594-600.

Congenital synostoses of the small bones of the wrist have been described; they usually are of no functional importance. Only once has a familial occurrence of such anomalies been reported. The author had an opportunity to examine members of three families with congenital aplasias of the interphalangeal joints, and observed synostoses of small bones of the wrist and foot in the same patients. It seems it is not the single type of synostosis that is hereditary, but rather the disturbance which leads to synostosis of any of the bones. The anomaly was found in the hand as often as in the foot.

HANS W. HEFKE, M.D.

ts
of
a-
nd
ie
en
ed
al
se
es
ts
es
ed
nd

he
ir-
6,
ist
al
of
p-
h
d
ot
pe
is-
es.
he